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An Address.[1]

RESEARCH AND THE GENERAL PRACTITIONER.

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President of the South Australian Branch of the British Medical Association.

THROUGHOUT HISTORY, periods of rapid progress have alternated with quieter intervals during which the social pattern has had time to adjust itself to new conditions. I believe we are living in such an interval at the present.

During the past twenty years it has been necessary for the medical profession to devote itself almost entirely to absorbing many revolutionary advances. This has been done very well indeed by those working in specialized fields; but little consideration has been given to the impact of these changes on the pattern of medical care as a whole. In this regard, an increasing amount of attention is being given to the place of the general practitioner in our profession. Interest in this question has been so widespread that John Hunt has suggested that we are seeing a "renaissance of general practice" which, in his words, is being expressed as "a world-wide movement concerned with the academic welfare and scientific encouragement of the family doctor".

It is not possible to discuss, within the limits of this address, all the avenues which are being explored by general practitioners to fit themselves to meet the demands of the future, so I will restrict myself to the part they can play in medical and sociological research.

In the first place, it must be recognized that medical advances and social progress have had the effect of placing many diseases and a multitude of social problems under the almost exclusive care of the family doctor.

Whenever significant progress has been made, the outlook of our profession to disease has undergone a series of changes. At first, enthusiasm for the new has resulted in extravagant claims such as those made seventy years ago by Southwood Smith, when he affirmed that "the panacea for ill-health was sanitation, disease disappearing as soon as bad sanitary conditions were corrected and never appearing while they were good".

Later, the effect of attention to environmental factors in the prevention of disease was seen in its true perspective, and today we no longer regard sanitation as the answer to all our problems.

[1] Read at the annual meeting of the South Australian Branch of the British Medical Association on June 24, 1959.

In more recent times we have seen the same thing happen with the introduction of life-saving drugs and modern techniques—so much so that the attention of medical men has tended to narrow down to a consideration of disease alone. As a result, our thinking has become clouded in relation to man himself and the many problems which beset him in his everyday life. In addition, we have failed to appreciate fully how much the pattern of disease has altered during the past twenty years. Many conditions, formerly common, are now rare; others, previously serious, are so modified that they are usually dealt with by the family doctor alone. In place of these problems others have become more apparent. These include a vast range of social, emotional and psychological factors, which have so far defied adequate classification. We speak of them as stress or psychosomatic diseases, hiding our confusion, as doctors often do, with phrases the meaning of which we do not fully understand.

In the midst of this apparent chaos, one thing stands out clearly—that there is ample scope for the family doctor to make his contribution to research. In the past, general practitioners have added to our store of clinical knowledge by studying the natural history of disease. The investigations of McKenzie and Pickles in Britain, and of Swift and Hone in this country, are well-known landmarks in this type of research. As long as disease affects man, there will be opportunities for such studies, and general practitioners, so minded, must be encouraged to make these observations.

Another type of research which needs our attention concerns the organization of general practice. Whilst no single pattern is suitable for all Australian conditions, the general principles which should guide all planning must be clearly defined.

Two objectives are particularly important if the family doctor system of practice is to survive. First, the main purpose of any planning must be to encourage steadily improving standards of service, and secondly, the practitioner must be able to treat his patients as individuals requiring continuity of care.

Whilst the opportunities which exist for research in these categories are recognized, the great challenge to the family doctor of the future is presented by those conditions in which both somatic and psychological factors play a significant part. These have been well described as "the uncultivated field of general practitioner research".

Precise evaluation of all the material of this type available in general practice today is still not possible. Before this can be done, we must understand more fully the implications of advances made in fields other than those we regard as purely medical. Whilst we readily apply the relevant discoveries of the physical scientists to the investigation and treatment of organic disease, we are much more guarded in our approach to the findings of the biologist and the social anthropologist. One reason for this, undoubtedly, is that the routine application of the techniques used by these workers has not been adequately studied under general practice conditions. However, investigations are now being made into this aspect, and one such inquiry is in progress in a country district of this State. It is obvious that, in many investigations, practitioners will need the help of research scientists. In Britain, these workers have shown that they are anxious to cooperate. They have given assistance with the design and planning of projects, and they have shown how, in many instances, the principles and techniques of modern investigation can be applied in the field.

In some projects, scientists and family doctors have worked together in the one team, as happened when Robert Cruikshank conducted his "Family Studies of Respiratory Infections". Throughout the English-speaking world, these two groups are coming closer together, and this is a happy augury for the future of medical research generally. One factor in the successful work being done for agriculture in this country is the good relations which exist between agricultural scientists and farmers. I am certain that general practitioners will be ready to play their part, in like manner, with medical scientists.

The idea of general practitioners' banding themselves together to investigate disease is not a new one.

> As early as 1880 the British Medical Association in London interested itself in collecting information on a large scale concerning disease and, during the years 1883-1888, special volumes were published describing collective investigations made by doctors in Great Britain. At one stage the wave of interest created by these studies spread to the Continent and even to America and India.

This wave of enthusiasm, however, died out, and it is important for us to realize that failure was the result of bad planning. If the present wave of interest in general practitioner research is to survive, we must ensure that the work is guided by a competent research organization.

In our consideration of such an organization, we can be assisted by the experience gained in these matters in Britain during the past five years. In that country, the College of General Practitioners soon after its foundation established a committee to inspire and coordinate research. This body, with Dr. Robin Pinsent, a Birmingham general practitioner, at its head, has developed a programme of projects in which some 700 doctors are engaged. Of these doctors, 108 have recently completed a twelve-month survey of the diseases found in general practice. The information collected by this morbidity survey is now being published in three "Grey Books" by Her Majesty's Stationery Office. This will provide a valuable basis for planning further investigations into the problems seen by general practitioners in Great Britain.

Another objective achieved by this committee is the establishment of an "Epidemic Observation Unit". This is designed "to locate an outbreak of some undiagnosed disease, define its clinical features and, with laboratory help, determine its cause". This unit functions continuously, sifting and analysing the information it receives and sending out advice concerning the incidence and nature of the infectious disease in question. The work of this service, apart from its research value, emphasizes the important part which can be played by the family doctor in modern preventive medicine.

Amongst the many contributions made by workers in Britain, their guidance on the principles which should govern our attitude towards research has been particularly helpful. They have emphasized that it is necessary for general practitioners to accept the discipline required for work of this nature, whilst recognizing at all times the limitations imposed by the conditions under which they work. It is important that the scope of their research is clearly defined, so that there is no wandering into fields more appropriate to the medical scientist. The acceptance of these principles will help allay any fears that these activities by general practitioners are a challenge to established research organizations.

Soon after general practitioner research revived in Britain, interest spread to New South Wales and Queensland. In these States, organized research is now well established, and groups of doctors have investigated a variety of problems, including the incidence and clinical features of infective hepatitis and eclampsia. Recently, research work has commenced in the other States, and with the formation of the Australian College of General Practitioners in 1958, planning has been proceeding on a Commonwealth-wide level.

As in Britain, it has been found that general practitioners interested in research can be classified into three groups.

> There is the lone worker who pursues a particular investigation within his own practice. A second, whilst willing to observe and record, is content to let others analyse the material and formulate conclusions. The third type is interested in a wider class of investigation involving a number of practices and requiring a team for his purposes.

Each of these types has a contribution to make which can be developed and assisted by satisfactory organization. So that we can take full advantage of the store of knowledge available in Britain, a Sydney general practitioner, Dr. John Radford, is at present in that country studying

the philosophy and organization of general practitioner research. This journey, made possible by a Pfizer Travelling Scholarship and assistance from the Post-Graduate Medical Foundation of New South Wales, is a practical expression of the widespread interest which is arising in this work.

In Australia today we are in the midst of many changes, and the future of our medical services has still to be determined. Medicine is a free profession, and to keep it so we must remain a united one. No one group must be allowed to lag behind in any way.

At the moment, one of our urgent problems concerns the place which general practice should occupy in Australian medicine. If this is to be a worthy one, it must be able to take its proper place alongside other groups by virtue of the contributions it makes in its own field. In this respect, general practitioner research, by providing an academic and scientific leaven, can play an important part. In addition, it can provide a bond of interest uniting all sections of the profession in a common task. To do this in a practical manner, it is necessary for all doctors to widen their concept of research. It should not be regarded as the privilege of the few, but as the duty of the many.

The multitude of human and clinical problems inherent in medical practice today makes it essential that all who accept the challenge between man and disease must play some part in this quest. We must remember always that "three great problems should dominate the thinking of a doctor—the nature of life; the nature of disease; and the nature of man".

Acknowledgements.

This address is based on material obtained from the "Research Newsletters of the College of General Practitioners", numbers 1 to 17, and *The Journal of the College of General Practitioners* and "Research Newsletters", numbers 18 and 19. Particular reference has been made to "The Lloyd Roberts Lecture" (1957) by John H. Hunt in *The North-West England Faculty Journal, College of General Practitioners*, Special Issue, 1957. The concluding quotation is taken from *Disjecta Medica*, selected by Orde Poynton, M.A., M.D., published by the Hassell Press, Adelaide, in 1954.

BONE MARROW TREPHINE BIOPSY: ITS DIAGNOSTIC VALUE, WITH PARTICULAR REFERENCE TO THE MALIGNANT LYMPHOMAS.

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BONE MARROW BIOPSY is an important method of investigation of disorders of the blood. There are two main methods of biopsy: (i) Aspiration (needle) biopsy, in which the bone marrow is aspirated through a specially constructed wide-bore needle; films of the aspirated marrow are then made on glass slides and stained like blood films, with a Romanowsky stain. When a sufficient number of fragments are aspirated, histological sections of the fragments can be prepared, if indicated (Raman, 1955). (ii) Trephine biopsy, in which a specially constructed trephine is used to obtain a biopsy specimen, from which a histological section is prepared.

In most disorders in which bone marrow biopsy gives diagnostic information, aspiration (needle) biopsy is preferred to trephine biopsy, not only because it is simpler, but also because it gives more information (de Gruchy, 1958). However, in certain cases, trephine biopsy will establish the diagnosis when aspiration has failed to do so; it is of particular value when aspiration has yielded only a "dry tap" or a "blood tap".

[1] Supported by a grant from the Anti-Cancer Council of Victoria.

It is the purpose of this paper to describe a method of trephine biopsy and to indicate its diagnostic value, particularly in the malignant lymphomas.

Biopsy Needle.

The aim of trephine biopsy is to obtain, with minimum discomfort and inconvenience to the patient, a sample of bone marrow tissue which is sufficiently large to permit adequate histological examination.

Several needles have been designed for bone marrow trephine biopsy. In 1943 Türkel and Bethell described a trephine for use on the sternum, which has the advantage that it can be used in the ward, but the disadvantage that it yields a biopsy fragment which is often too small for adequate histological examination; further, the fragment may break up while being prepared for sectioning (Dacie, 1956). Bernstock and Sterndale (1951) have also described a needle suitable for both marrow biopsy and aspiration, but the biopsy specimen is relatively small. More recently, McFarland and Dameshek (1958) have used the Vim-Silverman needle for marrow biopsy; the average specimen obtained by their methods measures 1·0 to 1·5 cm. in length.

During the past four years we have been using the trephine designed by Sacker and Nordin (1954) for iliac crest biopsy and have obtained satisfactory specimens with it. They describe the trephine as follows:

> The instrument consists of three parts: an outer sheath serrated at one end to grip the periosteum and flanged at the other end to provide an adequate finger-grip; a tubular trephine sharply toothed at one end, and provided with a milled head at the other; and a central trocar for ejecting the bone sample. The trephine is made of stainless steel, and the other two parts are chromium-plated.

Their paper gives an illustration of the instrument and the name of the maker.

When we first used this trephine we found that the biopsy specimen sometimes remained within the bone after withdrawal of the trephine from the bone; for this reason we now use with the trephine an adapter by which suction can be applied while the plug of bone is being loosened (Figure I). The adapter, made of stainless steel, is 2 cm. long and is designed to fit at one end onto a metal-tipped Luer (no lock) 20 ml. syringe, and at the other end into the open end of the trephine needle (see description of technique).

Technique.

There are many aspects of technique common to both marrow aspiration and trephine biopsy; it is therefore advisable, whenever possible, for the trephine biopsy to be performed by a clinical pathologist. Furthermore, the clinical pathologist is in the best position to know from the clinical, peripheral blood and marrow aspiration findings the indications for and the possible complications of trephine biopsy in a particular patient.

The patient is given a sedative, and preferably an analgesic also, one hour before biopsy.

Site of Biopsy.

Biopsy can be performed on either the anterior or the posterior iliac crest. However, in general, the posterior crest is preferred for the following reasons: (*a*) the procedure cannot be seen by the patient, (*b*) the cortical bone is thinner than on the anterior crest and thus less pressure is required for penetration, and (*c*) there is a greater volume of marrow at this site. Therefore, it is our routine practice to use the posterior iliac crest. Nevertheless, when there is evidence suggesting focal involvement (e.g., local tenderness to palpation or radiological change) elsewhere on the iliac crest, biopsy is performed at the site of this change, as biopsy at such a site is more likely to yield diagnostic material.

Method.

The procedure is performed in a minor operating theatre, with strict sterile technique. Gloves are worn

by the operator, who scrubs as for all surgical procedures. The patient is positioned on his side with knees drawn up and back flexed as for a lumbar puncture. The prone position may also be used, but it is less satisfactory in obese patients. The skin is prepared with a suitable antiseptic, and then the skin, subcutaneous tissues and periosteum are infiltrated with a local anæsthetic such as "Xylocaine". The periosteum is anæsthetized over the whole width of the iliac crest and for 2 to 3 cm. in its long axis; adequate anæsthesia of the periosteum is particularly important in preventing discomfort.

A short incision of about 1 cm. is made in the skin; the instrument is inserted through this incision down to the bone, until the serrations of the sheath are firmly impaled against the bone. Then, with the outer sheath held firmly by one hand, the trephine is rotated alternately in clockwise and anticlockwise directions to penetrate the periosteum and cortex; it is usually possible to tell when the trephine enters the medulla as a distinct lessening of resistance is felt. The standard trephine is so constructed that it penetrates into the bone marrow to a distance of 12 mm.; we have shortened the outer sheath of our instrument by 3 mm., thus allowing the trephine to penetrate to a distance of 15 mm. When the trephine is fully introduced it is gently rocked to loosen the plug of

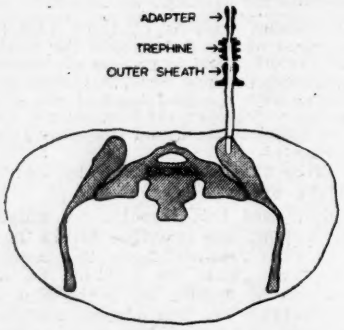

FIGURE I.

Diagram to show the trephine, with the adapter attached, in place in the posterior iliac crest. The relation of this part of the crest to the sacrum and the sacro-iliac ligament can be seen. The transverse section of the pelvis at the level of the first sacral segment is drawn approximately to scale; the trephine, however, is not drawn to scale.

bone it contains. At the same time suction is applied by a well-fitting 20 ml. syringe attached to the open end of the trephine by means of the special adapter. The trephine is then gently withdrawn, suction being maintained during withdrawal. After withdrawal, the trocar is inserted into the trephine to dislodge the biopsy specimen.

Pressure is then applied to the biopsy site until oozing ceases, when the skin is sutured. It is advisable to apply pressure for a further five minutes after the skin is sutured, as this lessens the risk of hæmatoma formation.

Complications.

The procedure is relatively simple and safe. It causes little discomfort provided that the periosteum is adequately anæsthetized; however, occasionally discomfort is felt as the trephine passes through the cortex or into the cancellous bone, especially in patients with bone pain or tenderness. It is noteworthy that some patients have volunteered the information that they had found previous sternal marrow aspiration more uncomfortable.

Possible complications are infection and hæmorrhage, but these should not occur if proper aseptic precautions are taken, and if adequate pressure is applied to the biopsy site. Thrombocytopenia is not a contraindication, provided that adequate pressure is applied to prevent hæmatoma formation.

Preparation of the Histological Section.

As soon as the biopsy specimen is removed from the trephine, one or two marrow particles are dislodged from it on to glass slides, and films are made and stained in the usual way; however, with fibrotic and infiltrated marrows, it is not always possible to obtain particles for films. When indicated, bacteriological studies (smears and cultures) are also performed.

The specimen is then used to prepare histological sections by the following technique, which in our hands has given the most satisfactory results.

The specimen is fixed in Heidenhain's "Susa" solution, which also acts as a decalcifying agent for a small piece of bone of this size; the time necessary for decalcification varies from two to four days; for specimens thought to be sclerotic, at least four days are required. After fixation and decalcification, the specimen is prepared for section in the following steps: (i) it is transferred to absolute alcohol plus sufficient iodine to make the solution brown (a few drops of saturated solution of iodine in absolute alcohol are used), and left for three hours; (ii) it is transferred to a fresh solution of absolute alcohol for three hours; (iii) it is placed overnight in a 5% solution of celloidin in equal parts of absolute alcohol and ether; (iv) the excess celloidin is poured off and a small amount of chloroform is added to harden the remaining celloidin; after a few minutes the specimen is gently loosened and the chloroform poured off; (v) the specimen is placed in two changes of benzene each for three hours; (vi) it is left overnight in paraffin at 56° C.; (vii) it is blocked in fresh paraffin and sectioned. Longitudinal sections are then cut at two different depths in the block, the second being that of the greatest diameter of the specimen. In certain cases serial sections are cut (see discussion). The length of section varies from 10 to 15 mm. and the width from 2 to 5 mm. In general the tissue pattern is well preserved, although there is commonly slight distortion at the sides of the section, due to traction at the time of biopsy and shrinkage during preparation. The sections are routinely stained with both hæmatoxylin-eosin and reticulin stains. If indicated, Gram and Ziehl-Neelsen stains are also used.

Results and Comment.

The main indication for marrow trephine occurs when aspiration at one or more sites has yielded a "blood tap" (blood alone, usually in small amounts, without marrow fragments) or a "dry tap" (no aspirate at all). It is also occasionally indicated in cases of suspected malignant lymphoma or tumour, when aspiration has yielded cellular but non-diagnostic marrow films. We have performed marrow trephine biopsy in 18 cases of "dry tap" or "blood tap" in which diagnosis had not been established; the trephine biopsy established the diagnosis in 17 out of these 18 cases. The causative disorders are listed in Table I.

The disorders in which marrow trephine biopsy may be of diagnostic value and the results of biopsy in our cases will now be discussed.

Malignant Lymphoma.

The diagnosis of malignant lymphoma can be established only by biopsy of one of the involved organs. In most cases, there is enlargement of one or more groups of superficial nodes, and biopsy of these nodes establishes the diagnosis; therefore, examination of the marrow is not usually required for diagnosis. However, it is not uncommon for lymph node enlargement to be absent at the time of presentation, and thus biopsy of another organ or tissue is necessary; in such circumstances marrow biopsy may yield a specimen suitable for histological diagnosis.

In general, marrow aspiration does not establish diagnosis in the malignant lymphomas, even when infiltration of the marrow is present. This is because (a) the infiltration often results in a "dry tap" or "blood

tap" and (*b*) even when marrow fragments are obtained, it is usually not possible to make a diagnosis by examination of a stained film (de Gruchy, 1958). However, occasionally histological examination of sections made from aspirated fragments is diagnostic (Pettet *et alii*, 1955).

In contrast to marrow aspiration, marrow trephine commonly yields diagnostic material in cases of lymphoma with marrow infiltration. In our series the diagnosis of malignant lymphoma was established by trephine biopsy in six cases, five of Hodgkin's disease and one of reticulum-cell sarcoma. Five of these cases showed no

TABLE I.

Results of Bone Marrow Trephine Biopsy in 18 Cases of "Dry Tap" or "Blood Tap".

Trephine Biopsy Diagnosis.	Number of Cases.
Malignant lymphomas:	
(*a*) Hodgkin's disease	5
(*b*) Reticulum-cell sarcoma	1
Myelosclerosis	9
Aplastic anæmia	2
Diffuse fibrosis of uncertain ætiology	1

superficial lymph node enlargement; in one the cervical lymph nodes were enlarged and biopsy had been performed, but histological examination had shown only non-specific hyperplasia. In all cases marrow aspiration had yielded a "dry tap" or "blood tap".

Four of these cases had presented with febrile splenomegaly and two with "refractory" anæmia. Clinical details are summarized in Table II, and the histories of two typical cases are set out below.

CASE I.—Mrs. A., a housewife, aged 48 years, was admitted to hospital on March 13, 1957, with a history of malaise and pain in the abdomen and in both legs for one week. Examination revealed a healthy looking woman with a temperature of 101° F. and a pulse rate of 100 per minute. Her spleen was slightly enlarged, but not tender; there was no icterus, hepatomegaly, superficial lymph node enlargement or cardiac bruit. There was tenderness to firm pressure over the sacrum, but no sternal tenderness. X-ray films of the chest, lumbar part of the spine and pelvis showed no abnormalities. Examination of the cerebro-spinal fluid showed a protein value of 80 mg. per 100 ml. and a lymphocyte count of 15 cells per cubic millimetre. The Paul Bunnell test and the typhoid and brucella agglutination tests gave normal results. The total serum protein content was 6·1 grammes per 100 ml., the serum albumin 3·1 grammes per 100 ml. and the globulin 3 grammes per 100 ml.; the serum bilirubin content was 1·0 mg. per 100 ml., the alkaline phosphatase level was 9 King-Armstrong units per 100 ml. and the cephalin flocculation test gave a positive result. An attempt at blood culture produced no growth. Examination of the fæces for E.C.H.O. and poliomyelitis viruses gave negative findings. Blood examination showed a hæmoglobin value of 12·1 grammes per 100 ml., a white cell count of 6000 per cubic millimetre (a differential count showed a mild neutropenia—2000 per cubic millimetre), a platelet count of 200,000 per cubic millimetre, a reticulocyte count of 3·7%, and an erythrocyte sedimentation rate of 10 mm. in one hour (Westergren). In the blood film, the red cells showed mild anisocytosis and microcytosis; initially there were no immature leucocytes and no nucleated red cells, but after several weeks these appeared in small numbers and at the same time a mild anæmia developed. The direct Coombs test gave a negative result and the red cell osmotic fragility was normal. Aspiration biopsy of the sternum yielded a "blood tap" without marrow fragments; a small number of atypical reticulum cells were seen in the film made from this blood. Trephine biopsy was performed on the right posterior iliac crest; the biopsy specimen showed the typical histological features of reticulum-cell sarcoma.

Comment.—This woman presented with the diagnostic problem of a febrile patient with splenomegaly and no lymph node enlargement. Investigation failed to reveal any infective process. Initially her blood examination showed only a mild neutropenia, but during observation she developed a leucoerythroblastic anæmia; this type of anæmia, together with back pain and sacral tenderness in a patient with febrile splenomegaly, suggested the possibility of malignant lymphoma with marrow infiltration; a "blood tap" on marrow aspiration with a small number of atypical reticulum cells supported this diagnosis, which was then established by marrow trephine biopsy.

CASE V.—Mrs. E., a housewife, aged 56 years, was admitted to hospital on January 10, 1958, with a 12 months' history of weakness and easy bruising; a diagnosis of pernicious anæmia had been made at the time of onset of symptoms. There was no lymph node enlargement, splenomegaly, hepatomegaly or bone tenderness. Blood examination revealed the following: a hæmoglobin value of 5·3 grammes per 100 ml., a white cell count of 4300 per cubic millimetre (neutrophil polymorphonuclear cells, 2100 per cubic millimetre), a platelet count of 50,000 per cubic millimetre, a reticulocyte count of 5·2% and an erythrocyte sedimentation rate of 31 mm. in one hour (Westergren). In the blood film the red cells showed moderate anisocytosis with macrocytosis, and poikilocytosis with many oval and pear-shaped cells; no nucleated red cells or immature leucocytes were

TABLE II.

Malignant Lymphoma Diagnosed by Marrow Trephine Biopsy.

Case Number.	Sex and Age.	Presentation.	Superficial Lymph Node Enlargement.	Splenomegaly.	Blood Picture.	Trephine Diagnosis.	Comment.
I	F. 48	One week, fever and pain in legs.	Absent throughout illness.	Slight.	Initially mild leucopenia; later leucoerythroblastic anæmia.	Reticulum-cell sarcoma.	Presentation with febrile splenomegaly. Total duration of illness three months. Diagnosis confirmed at autopsy.
II	M. 35	Three months, cough and fever.	Absent throughout illness.	Slight.	Pancytopenia.	Hodgkin's disease.	Presentation with febrile splenomegaly. Total duration of illness, five months. Diagnosis confirmed at autopsy.
III	M. 51	Four months, weight loss, pruritus and anæmia.	Absent throughout illness.	Slight.	Macrocytic anæmia.	Hodgkin's disease.	Presentation with "refractory" macrocytic anæmia. Total duration of illness, 12 months. Diagnosis confirmed at autopsy.
IV	M. 15	One month, fever and weight loss.	Absent after nine months' observation.	Marked.	Mild normocytic anæmia.	Hodgkin's disease.	Presentation with febrile splenomegaly. Alive nine months after onset.
V	F. 56	One year, anæmia.	Absent throughout illness.	Absent, except once after transfusion.	Macrocytic anæmia.	Hodgkin's disease.	Presentation with "refractory" macrocytic anæmia. Total duration of illness, two years. Diagnosis confirmed at autopsy.
VI	M. 31	Three months, chest pain, pallor and fever.	Slight enlargement of neck and axillæ. Biopsy—non-specific hyperplasia.	Slight.	Leuco-erythroblastic anæmia.	Hodgkin's disease.	Presentation with febrile splenomegaly. Total duration of illness, 16 weeks. Diagnosis confirmed at autopsy.

seen. The direct Coombs test gave a weakly positive result and the red cell osmotic fragility was slightly increased. X-ray films of the chest, lumbar part of the spine and pelvis showed no abnormalities. The serum alkaline phosphatase levels and serum protein levels were normal.

Aspiration biopsy of the sternum yielded only enough blood to make one smear; there were no fragments on this smear, but a number of atypical reticulum cells were seen, some with two nuclei. Erythropoiesis was macronormoblastic in type. Iliac crest trephine biopsy revealed a very cellular non-fatty marrow, with diffuse infiltration with Hodgkin's tissue.

The patient was treated by repeated blood transfusions. She subsequently developed severe bone pain, but no radiological bony changes, and she died 12 months later from fulminating staphylococcal pneumonia. At autopsy there was extensive infiltration of the bone marrow by Hodgkin's tissue, in which were scattered numerous patchy areas of fibrosis; the spleen, mediastinal and para-aortic lymph nodes were only slightly enlarged, but on histological section showed infiltration with Hodgkin's tissue. The liver was not involved.

Comment.—This patient presented with symptoms of anæmia and a blood picture of a macrocytic anæmia with oval macrocytosis and poikilocytosis, suggesting a megaloblastic macrocytic anæmia. Marrow infiltration was suggested by a "blood tap" with a number of atypical reticulum cells, and diagnosis was established by trephine biopsy. It is of interest that at no time in the clinical course were the superficial nodes enlarged, that the spleen was palpable on only one occasion after blood transfusion, that the liver was not involved, and that no bony radiological abnormality could be demonstrated. It is also of interest that at autopsy the marrow was the main site of involvement, and that numerous patchy areas of fibrosis were present (see fibrosis of the marrow).

Myelosclerosis.

Trephine biopsy was performed on nine cases of myelosclerosis, in which marrow aspiration had yielded a "dry tap" or a "blood tap". The clinical features and blood picture were suggestive of myelosclerosis in all but two of these cases; in these two a diagnosis of malignant lymphoma seemed more likely before trephine biopsy established the diagnosis of myelosclerosis.

Fibrosis of the Marrow of Uncertain Ætiology.

Fibrosis of the marrow is one of the causes of "dry tap". In addition to the fibrosis associated with myelosclerosis, fibrosis may accompany a number of disorders which involve the marrow, including lymphoma, leukæmia, carcinoma and tuberculosis. Thus, Weisberger (1955) found that marrow section showed extensive non-diagnostic fibrosis in five of 24 cases of "dry tap"; one of these patients was subsequently found to have metastatic carcinoma in the marrow at post-mortem examintion, two subsequently developed acute monocytic leukæmia, one was found to have Hodgkin's disease by lymph node biopsy and one patient remained undiagnosed. In only one of our patients did trephine biopsy yield non-diagnostic diffuse fibrosis; he was an Italian who returned to Italy and for whom we have no definite final diagnosis, although the clinical and radiological features strongly suggested Hodgkin's disease.

In cases in which the first sections show only non-specific fibrosis, it is important that serial sections are cut, as these may include tissue diagnostic of the disorder causing the fibrosis. However, if serial sections fail to establish a diagnosis, marrow trephine at another site (e.g., the opposite iliac crest) or rib biopsy should be performed.

Aplastic Anæmia.

Trephine biopsy is only occasionally necessary for the diagnosis of aplastic anæmia, as in most cases, marrow aspiration will yield fragments from which a diagnosis can be established; this is especially so when aspiration is repeated in those cases in which it is initially unsatisfactory. Thus we found that in 21 consecutive cases of aplastic anæmia, aspiration established the diagnosis in 18; in the other three repeated aspiration yielded a "dry tap" or "blood tap" and diagnosis was established by biopsy; in two of these cases biopsy was performed by trephine, and in one case surgical rib biopsy was performed (before the introduction of trephine biopsy).

Secondary Carcinoma of Bone.

In general, marrow aspiration is more satisfactory than is marrow trephine in the diagnosis of secondary malignant disease of bone. Thus we have found that in 11 cases in which marrow examination established the diagnosis, tumour cells were identified in films made from marrow aspirate and trephine biopsy was not necessary. However, in occasional cases of secondary carcinoma, aspiration yields only a "dry tap" or a "blood tap" without tumour cells, either because of the sclerosis of the marrow or because of tight packing of tumour cells in the marrow; in such cases surgical trephine may establish the diagnosis (Weisberger, 1955).

Leukæmia.

Trephine biopsy is indicated only in the occasional case in which multiple aspirations have yielded a "dry tap" or a "blood tap" in a patient suspected of having leukæmia; it has not been necessary in any of our cases of leukæmia.

Disorders Associated with Granulomatous Lesions in Bone Marrow.

In a number of disorders including tuberculosis, histoplasmosis, brucellosis, sarcoidosis, infectious mononucleosis and malignant lymphomas, histological section of bone marrow may show the presence of focal lesions known as granulomatous lesions. Pease (1956) has defined a granulomatous lesion as follows:

> A nodule of macrophages which have enlarged to form epithelioid cells, surrounded by a peripheral zone of lymphocytes and in some instances plasma cells, eosinophils and fibroblasts. The epithelioid cells may enlarge and coalesce to form Langhans' giant cells; however, in some instances giant cells may not be observed. The granulomatous lesion may vary in size from a single nodule to a prominent nodule, the latter occurring when neighbouring lesions coalesce. The granulomas may vary from few to many in number.

Pease found that

> with the exception of tuberculosis, histoplasmosis and brucellosis, in which the causative organisms were seen and identified bacteriologically, the granulomatous lesions were not thought to have any distinctive histopathologic characteristics.

In cases of malignant lymphoma, these non-specific granulomatous lesions may occur in addition to the specific histological lesions of the underlying lymphoma. Thus, when the initial section shows only a non-specific granuloma, serial sections should be cut, as these may show the diagnostic features of the causative disorder. This point was well illustrated by Case IV of the malignant lymphomas; the first section cut showed only several non-specific granulomas, but two further sections from different parts of the block showed the typical features of Hodgkin's disease.

Discussion.

There are several further points which require discussion.

Histological Interpretation.

Examination of all the biopsy specimens was performed by Dr. Sheila Clifton, pathologist, St. Vincent's Hospital, Melbourne. Dr. Clifton found that the biopsy specimens were of adequate size; however, she commented that in the malignant lymphomas histological interpretation of marrow sections was somewhat more difficult than that of lymph node sections.

Marrow Trephine Biopsy versus Needle Biopsy of the Liver in the Diagnosis of Malignant Lyphoma.

It has been pointed out that marrow trephine biopsy is especially helpful in the diagnosis of those cases of malignant lymphoma in which there is no enlargement of superficial lymph nodes. The liver is an alternative

organ for biopsy in such cases (Sherlock, 1958). In all six cases of malignant lymphoma, the liver was clinically palpable; however, in only two of five examined at autopsy was there evidence of infiltration with lymphomatous tissue; furthermore, in three cases liver biopsy was contraindicated because of thrombocytopenia. Thus, this small series would suggest that, in general, marrow trephine is preferred to liver biopsy, not only because it more often yields diagnostic material, but also because it is safer.

Trephine Biopsy versus Rib Biopsy

Until the introduction of the Sacker-Nordin needle, it was our custom to perform a rib biopsy (resection of a small segment of rib under general anæsthetic) when a histological section of marrow was required; this procedure gives a most satisfactory specimen for examination, but is more troublesome and more liable to complications than is trephine biopsy. We now consider that rib biopsy should be reserved for those cases in which trephine biopsy shows definite but non-diagnostic changes (e.g., fibrosis) and a larger specimen is required.

Trephine Biopsy in Metabolic Bone Disease.

We have used marrow trephine biopsy mainly for the investigation of disorders involving the bone marrow. However, it can also be used in the diagnosis and investigation of metabolic bone disease; thus we have found it helpful in a case of hyperparathyroidism presenting with renal calculi and no radiological bone changes and in which the biochemical findings were equivocal. It has also given confirmatory diagnostic evidence in a case of idiopathic steatorrhœa with osteomalacia and in a case of Paget's disease localized to the pelvis.

Summary.

A method for trephine biopsy of the bone marrow with the use of the Sacker-Nordin needle is described. The method includes the use of an adapter fitted to the needle, to ensure satisfactory withdrawal of the biopsy specimen from the bone.

The operation causes little discomfort to the patient, provided that the periosteum is adequately anæsthetized; it can be performed as an out-patient procedure. The posterior iliac crest is, in general, the most satisfactory site for biopsy.

The diagnostic value of marrow trephine in the investigation of patients with suspected marrow involvement, in whom marrow aspiration has yielded a "dry tap" or a "blood tap", is discussed.

The particular value of this technique in the diagnosis of malignant lymphoma without superficial lymph node enlargement is stressed.

Acknowledgements.

We are much indebted to Miss Nan Carroll, who prepared the histological sections, and to Dr. Sheila Clifton for her constant assistance and advice. We are also indebted to Associate Professor L. Ray and Dr. A. Roche, for their helpful advice on the anatomy of the iliac crest.

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CLINICAL FEATURES OF OVERT VIVAX MALARIA SEEN IN AUSTRALIA: INFECTIONS ACQUIRED IN NEW GUINEA.

By ROBERT R. H. BLACK,

School of Public Health and Tropical Medicine, Sydney.

THE European population of Papua and New Guinea is steadily increasing—it is of the order of 17,500—so that increasing numbers of people return to Australia each year either on leave or having completed their service in that Territory. In addition, there are quite a number of tourists or short-term visitors. Many of these people are exposed to malaria infection whilst in New Guinea. Suppressive drugs, if taken regularly, keep them free from malaria in New Guinea, and sometimes the first attack of malaria is experienced after their return to Australia.

Vivax malaria was a familiar clinical entity in Australia during and for a few years after the war amongst troops who had served in New Guinea; the uniform or service badge was a pointer to the diagnosis. At the present time malaria is an uncommon disease, and this may lead to delay in diagnosis unless it is remembered that quite a number of people living in Australia have recently been in New Guinea. In former times the patient—if he bothered to consult a medical attendant—came with the diagnosis ready made. With modern effective suppressive drugs the patient may be unable to offer this assistance in diagnosis. If he is seen during an influenza epidemic or if there are a few physical signs in the chest, an error may be made in diagnosis.

Delays in diagnosis of malaria in Australia have extended over periods of up to six weeks. Fortunately, vivax malaria is not a killing disease, but if the parasite responsible happened to be *Plasmodium falciparum*, the outcome would very often be fatal in a much shorter time than six weeks.

The features of overt vivax malaria presented here have been observed mainly in administration personnel and their wives during the last three years.

Time of Onset in Relation to Return to Australia.

Suppressive drugs may be taken for a variable period of time after return to Australia. If they are taken for a period of one month, subsequent attacks of falciparum malaria will be prevented. Amongst the patients concerned in this report suppressives have been taken for periods varying from one or two weeks to five or six months after leaving New Guinea.

Figure I shows the time of onset of malaria in relation to the time at which suppression was ceased. It will be seen that most cases occurred in the second month after the patient stopped taking his suppressive drug. However, an interval as long as nine months has been observed in this series in a patient who had left New Guinea more than a year before his attack occurred.

Incidence of Malaria in People Returning from New Guinea.

Little information is available on the incidence of malaria in people returning from New Guinea.

Amongst a group of 21 patrol officers at the Australian School of Pacific Administration, Mosman, who were observed for a period of almost one year, 11 developed overt vivax malaria. Five of these patients were married and their wives also developed vivax malaria. Patrol officers can probably be considered to be amongst those most exposed to malaria infection in New Guinea. At the other extreme are people who live permanently in Port Moresby and who do not leave the town area. Malaria would be unlikely to develop in such people after their return to Australia.

Symptoms.

The patients in the present series sought medical advice after the illness had lasted for periods of from a few hours to seven days (mean 3·2 days, if seeing the patient on the day of onset is counted as one day). Patients were frequently seen on the first, third or fifth day of their illness, periodicity of the symptoms being responsible for this phenomenon.

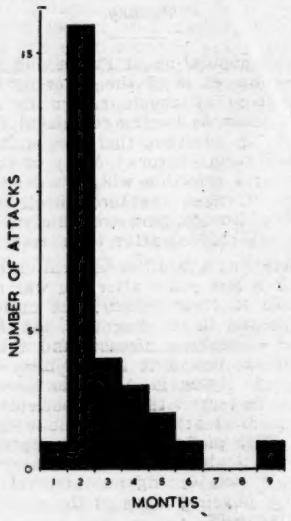

Figure I.

Time of onset of attacks of New Guinea vivax malaria in relation to the time at which suppression ceased in Australia.

Details of the symptoms of 28 patients suffering from overt vivax malaria are as follows. They were seen in Sydney and their infections were acquired in New Guinea.

Headache	27
Shivers	24
Rigor	5
Feverish and hot	17
Sweating	14
Aches and pains	21
Nausea	9
Vomiting	8
Weakness	3
Anorexia	3
Dizziness and giddiness	2

The common clinical picture was a patient who had headache, aches and pains in the back or limbs or both, and who felt shivery and later feverish. Sweating was usual, but rigors were not common. Fourteen of 18 patients showed periodicity in their symptoms, i.e., they felt well on the day between paroxysms; in 10 cases the history was of too brief duration for this to be evident.

Twenty-one of the patients gave a history of previous attacks of malaria while in New Guinea or while on leave from that Territory. In other words, this was the first attack of malaria for one-quarter of the patients.

Signs.

When the patients were first seen the temperature was recorded as normal in two cases. It ranged between 99° F. and 105·5° F. in 18 cases (commonly 102° F. to 104° F.). In eight cases the temperature was not recorded.

The spleen was palpable in 11 of the 21 patients in whom it was examined. It was Hackett Size I in six, and Size II in five patients. One of the larger spleens was tender. The liver was not enlarged in any of 19 patients in whom it was examined, but there was tenderness in the right hypochondrium close to the costal margin in two of these patients.

Relapses.

As these patients were given primaquine in an attempt to eradicate their infection, no information can be derived from this series on the incidence of relapse. However, some information is available from the history of these and other patients concerning the time intervals between attacks. This information is presented in Figure II for

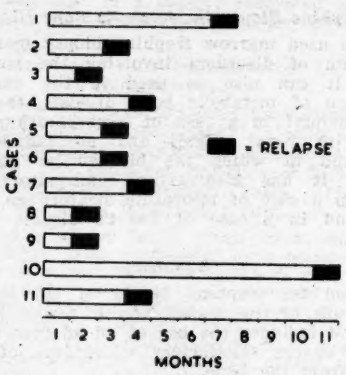

Figure II.

Intervals between attacks of New Guinea vivax malaria in Australia and first relapses.

cases in which no primaquine had been used, i.e., in which a trophozoiticidal drug only had been used for the treatment of the previous attack. It will be seen that the interval between attacks is commonly from two to four months—perhaps a little longer than the interval between the cessation of suppression and the subsequent attack of vivax malaria.

Differential Diagnosis.

A few of these patients became ill during an epidemic of influenza, and the diagnosis of influenza had been made either by themselves or by a medical practitioner. This is not surprising when the common symptoms seen in these cases are remembered. One case, in which vomiting was a feature, had been diagnosed as "gastric influenza". Two cases had been diagnosed as respiratory infection, but had not responded to penicillin. One of the female patients had been ill for two weeks. She was in early pregnancy, and had been treated for morning sickness and anæmia. She had a moderately heavy infection with *P. vivax* and a hæmoglobin value of 9·5 grammes per 100 ml. She responded rapidly to antimalarial therapy, and her pregnancy continued normally.

P. vivax was demonstrated in thick blood films in all 28 cases at densities varying from very scanty to five parasites per field of the thick film.

Treatment.

Chloroquine was used for the treatment of all patients, the course consisting of the following. On the first day, four tablets (600 mg. of base) at once and two tablets later in the day; on the second day, two tablets; on the

third day, two tablets. The patients were generally able to resume their usual activities on the second or third day of treatment.

Most of these patients were given a course of primaquine consisting of doses of either 15 or 22·5 mg. per day for 14 days and commencing on the same day as chloroquine therapy. The results of the use of primaquine for the eradication of vivax malaria of New Guinea origin are presented elsewhere. Here it is sufficient to note that the larger dose (22·5 mg. per day for 14 days) of primaquine reduces the incidence of subsequent relapses very significantly, but occasional relapses are seen after its use. Doses of 15 mg. per day for 14 days have been used in four pregnancies (one to seven months) with no ill effects.

Primaquine would not be indicated if the patient was returning within a few weeks to New Guinea. In these cases the use of a suppressive drug would be more appropriate.

Comment.

The material presented here requires little further comment. The importance of inquiry into a patient's previous places of residence has already been indicated. Malaria should be considered as a cause of pyrexia even in places where malaria is not endemic. The prognosis concerning subsequent relapses is much improved since primaquine has become available.

Acknowledgements.

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FOLLOW-UP INVESTIGATION OF ELEVEN CASES OF MILIARY TUBERCULOSIS AND TUBERCULOUS MENINGITIS.

By MARTHA RENTH,
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ISONIAZID is now recognized as the drug of choice in the treatment of all forms of tuberculosis, but when the first patients in this series started treatment, the value of isoniazid was still unproven.

This small series of 11 cases is presented for the following reasons: (i) all patients have been followed up for more than two years; (ii) all were treated with isoniazid; (iii) streptomycin, which was given intrathecally to the patients with meningitis, was stopped as soon as the patient came under my care; (iv) all patients were treated in a sanatorium as soon as transfer from the general hospital wards could be arranged.

The 11 patients presented here were all females, comprising those admitted for miliary tuberculosis and/or tuberculous meningitis to Fairfield Chest Unit, a sanatorium for females associated with the Fairfield Infectious Diseases Hospital, Melbourne. Their ages ranged from 15 years to 68 years, no children being admitted to this sanatorium. These patients can be divided into three groups: those with miliary tuberculosis (four cases), those with miliary tuberculosis and tuberculous meningitis (five cases), and those with tuberculous meningitis without miliary tuberculosis (two cases).

The first patient started treatment in March, 1952, and as her treatment set the pattern for the line of management in the following 10 cases, I shall briefly give her clinical record.

CASE I.—Mrs. A. was aged 36 years when she was admitted to the Queen Victoria hospital, Melbourne, on February 28, 1952, with pyrexia of eight weeks' duration. Her previous history was of pulmonary tuberculosis, which had been treated in a sanatorium in 1942, and of tuberculosis of the thoracic part of the spine with a transverse lesion of the cord, which had been treated by orthopædic measures in a sanatorium from 1946 to 1949. There were no residual neurological changes. X-ray examination of the chest on her admission to hospital showed appearances typical of miliary tuberculosis of the lungs.

Treatment was started immediately with streptomycin, one gramme daily, and thiosemicarbazone, 100 mg. daily. PAS in conjunction with streptomycin had been tried, but was not tolerated. Diagnosis was confirmed in due course by positive results to cultures of fasting gastric contents and urine, and by liver biopsy, which showed granulomata typical of tuberculosis. No choroidal tubercles were seen. Initial progress was satisfactory, except for intermittent headaches. Lumbar puncture was impossible because of gross angular kyphosis. On May 19, streptomycin was reduced to one gramme on alternate days, at which time she had received 74 grammes of streptomycin already, and thiosemicarbazone was continued as before. Headaches persisted, and the patient's condition deteriorated. Cisternal puncture was performed on June 12, and the findings in the cerebro-spinal fluid were as follows: 50 lymphocytes per c.mm., a protein content of 80 mg. per 100 ml., and a chloride content of 691 mg. per 100 ml. Cultures gave positive results for *Mycobacterium tuberculosis*, which was sensitive to 2 μg. of streptomycin. The dosage of streptomycin was increased to two grammes daily, and thiosemicarbazone (100 mg. daily) was maintained; 100 mg. of streptomycin were given by cisternal route on three occasions, and each time caused great distress—vertigo, nausea, vomiting and increase in the severity of headaches. The patient became drowsy and presented the typical picture of tuberculous meningitis in the final stages.

At that time samples of isoniazid had just become available and were kindly put at the disposal of Dr. Leslie Williams, who was in charge of the case. Dr. Williams discussed the situation with me, and we both thought that there was nothing to be lost in trying it, as the patient's fate seemed to be sealed with the present treatment, which had failed to control the disease. Fortunately the patient was still able to swallow, and treatment with isoniazid, 50 mg. three times a day, was started on June 23, all other treatment being stopped. Although on very small doses by present-day standards, the improvement in her condition was nothing short of miraculous. Within two weeks she was bright and talkative and she displayed a good appetite, and within six weeks she sat out of bed and was transferred to the Fairfield Chest Unit. Isoniazid levels were estimated and were as follows: in the urine, 64 μg. per millilitre, in the serum, 3 μg. per millilitre, and in the cerebro-spinal fluid, 3 μg. per millilitre.

Treatment with isoniazid, later on in conjunction with PAS, was continued for nine months in a sanatorium and for a total of 24 months as an out-patient. The cerebro-spinal fluid was normal after six months' treatment with isoniazid.

Encouraged by the experience with this first case, a further 10 patients with miliary tuberculosis with or without meningitis were treated with streptomycin, one gramme per day, and isoniazid, 5 mg. per kilogram of body weight in the years 1952 to 1953, and 10 mg. per kilogram of body weight thereafter. The patients with meningitis had only as much streptomycin given intrathecally as they had received before transfer to Fairfield Chest Unit, which amounted to 8 and 18 injections of 100 mg. to the patients in Cases III and V respectively. The patients in Cases VII, X and XI had no streptomycin given intrathecally, and the patient in Case VI is exceptional in so far as her treatment is concerned.

CASE VI.—The patient remained in the public wards for several months. Diagnosis was not established, although suspected, and she was treated accordingly with streptomycin, 250 mg. every six hours, isoniazid, 250 mg. daily, PAS, 12 grammes daily, and 16 intrathecal injections of 100 mg. of streptomycin. She developed papilœdema, external rectus paresis and epileptiform seizures. Diagnosis not having been established with certainty, craniotomy was performed. At operation miliary tubercles were seen in the Syvian fissure. A polythene tube was introduced into the interpeduncular fossa, and through this tube 75 mg. of streptomycin were introduced daily for 35 days. Systemic antimicrobial treatment was carried on for four months only, and she remained without effective treatment for six months. She was then transferred to Fairfield Chest Unit, where treatment with streptomycin and isoniazid was resumed, and her cerebro-spinal fluid became

normal five months later. She is the only patient in this series who has sequelæ in the form of temporal lobe epilepsy.

Treatment.

My reasons for not using intrathecal treatment with streptomycin since 1952 were based on the following considerations.

1. Streptomycin given intrathecally causes a local reaction with pleocytosis and can cause severe reactions, as could be seen in Case I. Yet, isoniazid levels in the cerebro-spinal fluid, equal to blood levels, were tolerated perfectly well.

2. Diffusibility of isonazid seemed to be very satisfactory, as suggested by the estimation of blood and cerebro-spinal fluid levels in Cases I and III. This assumption proved to be correct, as seen by reports appearing after 1952.

3. Repeated lumbar punctures in a seriously ill patient are an ordeal which should be reduced to a minimum. This was stressed by Professor Smellie in his report on the treatment of tuberculous meningitis in children, and applies equally to adults.

Diagnostic lumbar punctures only (or cisternal punctures in Cases I and VII, in which lumbar puncture was impossible) were performed at monthly intervals, and all seven patients showed progressive improvement. No spinal block developed in any case, but with the small number of patients treated, it is impossible to prove that this is due to the absence of chemical irritation by streptomycin or other factors.

Chemotherapy.

Chemotherapy consisted of streptomycin, one gramme daily for four weeks, then one gramme three times a week for eight weeks, together with isoniazid 5 to 10 mg. per kilogram of body weight daily. After three months this schedule was changed to isoniazid as before with 12 grammes of PAS daily. This was continued for 12 to 24 months, part of this being out-patient treatment. PAS was withheld at the start of treatment, as with other seriously ill patients, because it is badly tolerated, and when hydration and nutrition are in the balance it is not justifiable to use PAS, which causes nausea, vomiting and diarrhœa in a large number of patients. As regards the danger of emergence of resistant organisms, a period of three months' combined treatment with isoniazid and streptomycin is perfectly safe.

Treatment with isoniazid has the advantage, for which every clinician is truly grateful, of making the patient feel very much better in a comparatively short time. One is repeatedly surprised at the discrepancy between the clinical condition and the findings in the cerebro-spinal fluid, which in this series took from six to 18 months to become normal. Examples in this are the following two cases.

Case V.—The patient was given two weeks' Christmas leave, despite the fact that her cerebro-spinal fluid was grossly abnormal. She was taught to give herself streptomycin in this time and continued to take isoniazid. During these two weeks she became engaged and returned from leave none the worse for her exciting time.

Case X.—This patient was very ill on admission to hospital. She was vomiting and dehydrated, and she had papilloedema and cerebro-spinal fluid pressures of over 360 mm. of water. Within two weeks of starting treatment she asked permission to attend the weekly film night in the sanatorium.

Sanatorium Treatment.

No matter what its varied manifestations are, tuberculosis is one disease. It seems illogical to me that tuberculosis of the lungs should be treated in one type of institution and by one team of specialists, whilst any other manifestation of the same disease should be treated on completely different lines, depending solely on which anatomical system is affected. Sanatoria have a deservedly well-established place in the treatment of tuberculosis, and the advantages of organized rest and quiet, away from the hustle and bustle of the busy general wards, are probably best appreciated by the patients themselves, who never fail to express their appreciation of the change. Moreover, the long-term tuberculous patient, whether suffering from pulmonary tuberculosis, tuberculous meningitis, pelvic or orthopædic tuberculosis, should not be deprived of the advantage of being a member of the sanatorium community and should have full use of the facilities for rehabilitation as provided in sanatoria. In a general ward, the tuberculous patient is an odd case in a mixed community, whose problems and rehabilitation are generally not shared by the other patients. He consequently feels lonely and quite often is regarded with fear by fellow patients and even by nursing staff, whose knowledge regarding the infectivity of tuberculosis may be insufficient. Treatment in a sanatorium does not preclude closest liaison with specialists in the cases of extrapulmonary tuberculosis, and good teamwork here, as in other branches of medicine, assures the patient of planned, effective treatment.

Diagnosis.

Diagnosis was established by various investigations, as set out in Table I. All cases, except Cases VI and IX, had positive bacteriological findings. In Case VI miliary tubercles were seen at craniotomy and in Case IX X-ray findings only were positive. The husband of the patient in Case IX, who had "positive" sputum, had been admitted to a sanatorium two to three weeks prior to the patient's illness, and X-ray examination of her chest showed typical appearances of miliary tuberculosis.

Side Effects of Chemotherapy.

All patients displayed vestibular disturbances at the end of treatment.

Case II.—The patient was a known diabetic, and had peripheral neuritis, which was present at the onset of treatment with isoniazid. She was given regular injections of vitamin B complex, and treatment with isoniazid did not aggravate the condition, which we regarded as diabetic neuritis.

Case IX.—The patient developed a petechial rash after one month's treatment. Her hæmoglobin value was 76%, and white blood cells numbered 2800 per c.mm. (50% lymphocytes). Marrow puncture gave normal findings. We considered the neutropenia to be due to the disease, and continued with chemotherapy as before. The rash subsided and the blood picture became normal after a few weeks.

Follow-Up.

None of the 11 patients died of tuberculosis during a follow-up period of two to six years. None developed any manifestations of tuberculosis not present before their admission to hospital. This fact is particularly satisfactory in relation to the five cases of miliary tuberculosis and meningitis, which generally carry a bad prognosis.

One patient died of congestive cardiac failure 24 months after discharge from hospital. She was the patient in Case VIII, who had mitral stenosis, for which valvulotomy had been attempted two years before her tuberculous illness, but it had been unsuccessful.

The patient in Case III developed endogenous depression two years after discharge from hospital and responded well to psychiatric treatment.

Pregnancies.

The patient in Case IV had a twin pregnancy in 1957. The pregnancy was uneventful, but the twins died of prematurity (seven months). The patient in Case VIII is eight months' pregnant at the time of writing, and is perfectly well. The patient in Case IX was delivered of her third child in December, 1957. The patient in Case III had five children before the onset of her illness, and did not wish to undergo any more pregnancies. The patients in Cases I, X and XI are divorced. The patient

TABLE I.

Details Concerning the 11 Patients Treated and Followed Up.

Case.	Age. (Years.)	Miliary Tuberculosis.	Tuberculous Meningitis.	Source of Positive Findings.	Duration of In-Patient Treatment. (Months.)	Associated Diseases.	Length of Follow-Up.	Present Condition.	Total Chemotherapy. (Months.)
I	36	+	+	Urine, cerebro-spinal fluid, liver biopsy.	9	Pulmonary tuberculosis, tuberculosis of the spine.	6 yr.	Well, working.	24
II	68	+	–	Liver biopsy, gland biopsy.	10	Diabetes.	5 yr. 6 mth.	Reasonably well, aged 76 years.	7
III	31	+	+	Cerebro-spinal fluid.	12	—	5 yr. 6 mth.	Well.	18
IV	15	+	–	Urine, choroidal tubercles.	16	—	5 yr. 2 mth.	Well.	24
V	19	+	+	Cerebro-spinal fluid smear.	16	—	5 yr.	Well, pregnant.	24
VI	25	–	+	Craniotomy.	24	—	4 yr. 6 mth.	Well, temporal lobe epilepsy, fourth nerve palsy.	36
VII	60	+	+	Cerebro-spinal fluid.	14	Tuberculosis of the lumbar part of the spine, of the kidney and of the phalanx.	4 yr.	Well.	18
VIII	43	+	–	Fasting gastric contents, choroidal tubercles, urine.	12	Mitral stenosis, failed valvulotomy.	4 yr.	Died in 1957.[1]	12
IX	30	+	–	Chest skiagram only.	12	—	4 yr.	Well, delivered of her third child, December, 1957.	24
X	23	–	+	Cerebro-spinal fluid.	14	Pleurisy.	3 yr.	Well, working.	24
XI	35	+	+	Fasting gastric contents, cerebro-spinal fluid.	21	Tuberculosis of the sacro-iliac joint.	2 yr. 6 mth.	Well.	Still on chemotherapy.

[1] Death caused by mitral stenosis and congestive cardiac failure.

in Case VI had prolonged amenorrhœa after her illness. She started regular menstruation in December, 1955, but has not become pregnant. She has not been investigated as to the cause of her sterility as yet, but she may be considered the only patient out of eight patients of child-bearing age who is sterile. She has never had any signs of pelvic infection or miliary tuberculosis, and her sterility cannot necessarily be attributed to her illness.

Sequelæ.

One patient only (Case VI) has sequelæ in the form of temporal lobe epilepsy and paresis of the fourth cranial nerve.

Summary.

Eleven consecutive cases of miliary tuberculosis with and without tuberculous meningitis are presented.

All were treated with isoniazid in conjunction with streptomycin and later with PAS.

No streptomycin was given intrathecally to the patients with meningitis.

No patient died of tuberculosis.

All were treated in a sanatorium.

The follow-up has been two to six years.

Acknowledgements.

My thanks are due to Dr. Leslie Williams for her never failing and enthusiastic support and for her helpful criticism in the preparation of this paper; to Dr. R. Marshman, who made the first supplies of isoniazid available; and to my colleagues, who referred the patients to me.

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SULPHAMETHOXYPYRIDAZINE IN THE TREATMENT OF URINARY INFECTIONS.

By MICHAEL SALVARIS, F.R.C.S., F.R.C.S. (Edinburgh), F.R.A.C.S.,
Melbourne.

IN the treatment of urinary infections, many drugs and antibiotics whose antibacterial qualities have been proven have been employed in the past twenty years, but even with the advent of the antibiotics the sulphonamides still remain the most commonly used drugs in the over-all treatment of infections of the genito-urinary tract. It has been established that the indispensable immutable component of a bacterially active sulphonamide is the following chemical structure:

FIGURE I.

In this R is $-SO_2N$ (Sophian *et alii*, 1952). Many thousands of varieties of substitutes have been added to this group, many of which have antibacterial potency; but few have survived the critical analysis of continued therapeutic requirements.

In the choice of a sulphonamide drug, the efficacy of its antibacterial qualities cannot be the sole consideration. Many drugs of this group fulfil that requirement; but also other factors, which include satisfactory absorption, adequate solubility, good excretion, minimal toxic reactions and also the degree of acetylation, diffusibility and effect of combination with plasma proteins, play an

important part in determining the particular suitability of each individual member of the large sulphonamide group.

It is the purpoe of this paper to discuss the use of sulphamethoxypyridazine ("Lederkyn"), one of the more recent sulphonamide drugs. Experiments on dogs, rabbits and mice have determined the following qualities: high solubility in urine; good absorption from the alimentary tract; very slow urinary excretion; poor acetylation; and antibacterial activity equal to the better-known sulphonamides—e.g., sulphadiazine (American Cyanamid Company, 1956). Sulphamethoxypyridazine has been given in this series to 120 patients, and attempts have been made to determine its tolerance, its efficacy in treatment, its blood levels—and particularly in regard to the latter, the ability to sustain these levels at varying dosages. The ages of patients ranged from 18 to 82 years. Of the 120, 74 were males and 46 were females.

The Present Series.

The drug was used in the following circumstances: (i) in acute urinary infections, including acute pyelonephritis, acute cystitis, acute prostatitis, acute epididymo-orchitis; (ii) in chronic infections, including pyelonephritis or acute remissions of calculous pyelonephritis; after operations on carcinoma of the bladder with or without radioactive implants such as tantalum wire or radon seeds; after operations in the presence of established infections in the kidney—for example, nephrolithotomy or pyelolithotomy, pyeloplasty, ureterolithotomy; after partial cystectomy and before and after prostatectomy; in chronic cystitis and chronic cystourethritis; (iii) prophylactically, prior to or after instrumentation; (iv) in total cystectomy; it was given in three cases in which total cystectomy and ureteric transplant were performed, to observe the blood levels. When possible, both sensitivity tests and culture were carried out, and sensitivity of the infecting agent to sulphonamides was regarded as a prerequisite for those patients on whom therapeutic trials were carried out. Of the total number of patients treated, 60 were classified as suffering from an acute infection, 35 were classified as suffering from chronic infection, and 25 were given this drug prophylactically and for the other listed reasons.

The causative organisms were predominately Gram-negative, and included *Escherichia coli*, *Aerobacter aerogenes*, *Staphylococcus pyogenes*, *Staphylococcus albus* and occasionally *Streptococcus fæcalis*, *Proteus* and *Pseudomonas pyocyanea*.

In 100 cases, the average dosage employed was 2 grammes on the first day and 1 gramme on subsequent days. The dosage was divided into equal amounts and given twice daily at intervals of 12 hours. In 20 cases, the dosage of 0·5 gramme per day was given in two doses of 0·25 gramme each.

Blood Levels.

The efficacy of a drug and its dosage are estimated on a satisfactory blood level. This level is fairly constant for all the sulphonamide group of drugs, and has been estimated to be between 5 and 10 mg. per 100 ml. of blood for ordinary infections, and between 10 and 15 mg. for severe or gross infections (Grollman, 1951).

Blood levels were estimated in the following cases with varying dosages of sulphamethoxypyridazine. The levels were measured in terms of the total free drug and estimated by the Bratton and Marshall method. Tablets of 0·5 gramme each were used. The following figures represent the average blood levels at varying times.

One single dose of 4 grammes was given to three patients; the average blood levels (per 100 ml.) were as follows:

1 hour	after, ...	4	mg.
3 hours	after, ...	15·0	mg.
6 hours	after, ...	17·6	mg.
12 hours	after, ...	16·0	mg.
24 hours	after, ...	12·0	mg.
48 hours	after, ...	7·5	mg.
72 hours	after, ...	4·0	mg.
96 hours	after, ...	2·0	mg.

One single dose of 2 grammes was given to three patients; the average blood levels (per 100 ml.) were as follows:

1 hour	after, ...	3·6	mg.
2 hours	after, ...	6·8	mg.
4 hours	after, ...	14·6	mg.
8 hours	after, ...	12·9	mg.
12 hours	after, ...	11·4	mg.
24 hours	after, ...	8·3	mg.
48 hours	after, ...	3·1	mg.

When an initial dose of 2 grammes was given and followed by a maintenance dose of 1 gramme per day, given as two doses of 0·5 gramme each, the average of 60 blood level estimations in subjects aged from 18 to 80 years and weighing an average of 164 pounds, was 12·6 mg. per 100 ml. of blood. These tests were carried out between six and twelve hours after administration of the drug.

The above-mentioned blood levels would suggest that this dosage is rather too high for an average urinary infection, and it was decided to try a lower dosage.

A series of 20 patients were then given 0·5 gramme per day in divided doses of 0·25 gramme twice a day. The blood levels in these patients averaged 4·5 mg. per 100 ml. of blood. All these tests were carried out 12 hours after dosage. It would appear that a daily dosage of 0·5 gramme of sulphamethoxypyridazine is adequate from the point of view of blood levels.

The level of 4·6 mg. per 100 ml. represents the twelfth hour after oral administration, and is satisfactory. As will be shown, the response of urinary infections to this dosage compared favourably with the response to the higher dosage.

It is of interest to compare blood levels with those of the better-known sulphonamides, a much larger dose of which has to be administered to obtain similar blood levels; these are set out in Table I.

TABLE I.

Blood Levels of Some Other Sulphonamides.

Sulphonamide.	Initial Dose.	Blood Level. (Milligrammes per 100 Millilitres.)[1]	Remarks.
Sulphadiazine	3 grammes.	2·0 to 5·0 in 6 to 8 hours, and 1·0 to 2·5 after 24 hours.	A dose of 6 grammes per day provided a blood level of 9·5 mg. of free sulphadiazine per 100 mo. (Findlay, 1942.)
Sulphamerazine	3 grammes.	6·0 to 11·0 in 4 hours, and 2·5 to 4·0 after 24 hours.	A dose of 4 grammes per day provides a blood concentration of 9·8 mg. per 100 ml. (Lindberg *et alii*, 1946.)
"Gantrisin"	3 grammes.	4·8 after 4 hours, 4·2 after 8 hours, 4·1 after 48 hours.	A dose of 1 gramme per day for 2 days was required to keep the blood levels as stated. (Bryer *et alii*, 1948.)

[1] These estimates include the amount of free drug in milligrammes per 100 ml. of blood.

All sulphonamides undergo metabolism in the body as follows: (i) acetylation—conjugation with an acetyl group in the para-amino position; (ii) conjugation to form glucuronates, sulphates, etc.; (iii) oxidation.

The important change from the point of view of therapy and toxicity is the acetylation. Most acetyl derivatives of the sulphonamide group are comparatively insoluble and largely inactive antibacterially. The low solubility is of importance because of its consequent precipitation in the renal tubules with subsequent renal damage or other complications. The amount of acetylation in therapy was not estimated; but others (Frisk *et alii*, 1957) have given this figure as approximately

5%, and the solubility of the acetylated forms as approximately one third that of the drug itself.

The adequacy and relative rapidity of absorption of a drug, together with the effective maintenance of its concentration, are criteria of its therapeutic value. Sulphamethoxypyridazine given as a single dose of 4 grammes reached therapeutic levels in under two hours, with a maximum blood concentration in four to six hours, and maintenance of therapeutic levels continued for 48 hours. A single dose of the same drug of 2 grammes averaged a therapeutic level in under two hours, gave a maximum blood concentration in four to six hours and maintained a useful level for 24 hours. On a dose of 0·5 gramme per day, the level reached at the end of 12 hours was 4·6 mg. per 100 ml.

Urinary Levels.

The urinary levels were estimated in two cases only. These patients averaged 160 pounds in weight, and were each given 4 pints of fluid per day. The dosage used was an initial dose of 2 grammes and a maintenance dose of 1 gramme per day. An average of 15% was excreted after 12 hours, 28% after 24 hours, 50% in 48 hours and 75% after a period of 96 hours.

It is to be seen, therefore, that the excretion of sulphamethoxypyridazine is very slow, and thus the drug has a long action.

TABLE II.

Comparison with Other Sulphonamide Drugs.
(Sophian *et alii*, 1952.)

Sulphonamide.	Amount Excreted.	
	In 24 Hours.	In 48 Hours.
Sulphadiazine	50%	75%
Sulphamerazine	40%	60%
Sulphamezathine (after one dose of 3 grammes) ..	25% to 50%	72%
"Gantrisin"	39% to 93% in 24 to 48 hours	

Clinical Trials.

A series of 120 patients were given sulphamethoxypyridazine ("Lederkyn"). The drug was usually given over a period of seven days, but the longest time during which a patient received treatment was 30 days. The trial series included 25 who received it for prophylactic or diagnostic reasons.

Of the 90 patients in the first group, 60 received treatment for acute infections of the urinary tract; they were mostly suffering from primary infections, usually unassociated with any obstructive uropathy, which included chiefly acute pyelonephritis, acute cystitis, acute cystourethritis, acute prostatitis, epididymitis and epididymo-orchitis. The urine of all these patients was subjected to extensive investigations, including culture and sensitivity tests, and all patients selected for this study had infections in which the offending organism was sensitive to sulphonamides.

Thirty-five patients were listed as having chronic infections. They all had suffered from diseases of the urinary tract for periods varying from at least six months to many years. In this group were also included post-prostatectomy patients; but the majority had infections of a long-standing nature, including obstructive lesions of the urinary tract, radio-active implants and tumours of the bladder, and some patients were included for whom, for some reason or other, surgery could not be contemplated.

The offending organisms included *E. coli* (50 cases), *A. aerogenes* (8), paracolon bacilli (3), *Proteus* (4), *P. pyocyanea* (2), *Staph. pyogenes* (4), *Staph. albus* (13) and *S. fæcalis* (4).

Clinical improvement was judged in terms of symptomatic improvement, relief of accompanying pyrexia, or reduction of pyuria and sterility of subsequent specimens of urine.

Of the 60 patients with acute infections, 48 had completely recovered and were asymptomatic in three to seven days, with sterile urine. Eight patients improved clinically, but not all had sterile urine; in these mixed sulphonamide-resistant infections were found on subsequent tests, and other drugs of the antibiotic type were employed. The infections of four patients were unresponsive or became subsequently resistant to sulphamethoxypyridazine. These included two cases of recurrent epididymitis, one of cystitis and one of prostatitis.

The chronic urinary infections were, for the most part, unresponsive, as would be expected, but these patients were submitted to treatment when the organism or organisms (some were mixed infections) were sensitive to sulphonamides. These patients included those with long-standing calculous disease, neurogenic uropathies, obstructive lesions, radio-active implants, etc. The value of any drug in cases of this type is of little significance, for the infection will inevitably recur unless the causative lesion is adequately removed. The only point in including such patients in a clinical trial is, curiously enough, because they have chronic infections and the urine is infected all the time. Any temporary sterility of the urine is a more accurate guide to the efficacy of a drug against a particular organism than it is in the acute infections.

Of the 35 patients with chronic infections, clinical improvement was noted in 20; but of these, recurrences were noted subsequently in all but five of the 20. Fifteen had sterile urine for periods ranging from a few days to weeks; but return of the infection was inevitable, owing to reinfection either by the same organism or by another. At the time of writing, five patients only had not suffered such a recurrence.

Evaluation of Dosage.

The recommended dosage of 2 grammes *statim* and 1 gramme per day, was employed in 70 cases, but 20 patients were given a dosage of 0·5 gramme per day, and this dosage appears adequate to deal with the ordinary urinary infection. No percentage difference was noted clinically between the efficacy of the larger and that of the smaller dose; but in fulminating infections in which the risk is considerable, it would seem wiser to employ a daily dosage of at least 1 gramme, since the blood level is apparently twice as high, as might be expected, when 1 gramme is given as compared with 0·5 gramme.

No sulphonamide to date has been free from some reactions, and rarely are these due to overdosage. Sensitivity to the sulphonamide radical appears to be the causal factor. Indeed, the general opinion inclines towards the belief that an individual who is sensitive to one sulphonamide usually reacts in the same way to any member of the entire group (Sophian *et alii*, 1952).

With the reduced dosage of 0·5 gramme per day used in 20 cases, no untoward reactions were noted that could be specifically ascribed to the drug. Neither were there any indications to withdraw the drug. It seems likely that sulphamethoxypyridazine has no deleterious side effects in this dosage. When 2 grammes *statim* and a maintenance dosage of 1 gramme per day were employed, seven patients (5%) complained of headaches and nausea with or without vomiting. Two patients had skin rashes, one of sufficient severity to necessitate withdrawal of the drug. Two patients had bleeding per urethram; these were both post-operative patients, and bleeding may have been secondary. However, one of these two also had rectal bleeding, which continued until the drug was withdrawn. Examination of the blood of this patient revealed no structural abnormality. No crystalluria was noted. With regard to the hæmatopoietic effects, except for the two instances mentioned above, there were no specific indications to warrant special investigation of the blood, and this was not carried out as a routine measure.

Summary.

The value of sulphamethoxypyridazine in the treatment of urinary infections is discussed.

Estimation of blood and urinary levels indicates that the drug is absorbed adequately and excreted slowly.

A comparison is made with other sulphonamide drugs in more common use.

Clinical trials are evaluated: a dosage as low as 0·5 gramme per day appears adequate for the ordinary infection of the urinary tract.

The ability to act longer in smaller dosage suggests that sulphamethoxypyridazine has a useful place in the family of the sulphonamide group of drugs.

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PROVOCATIVE TESTS FOR GLAUCOMA.[1]

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THE functional efficiency of a tissue, organ or physiological system of organs may be assessed in a variety of ways. This paper is concerned with the tests employed to assess the functional efficiency of the organs and structures concerned with the maintenance and control of ocular tension. In particular, attention will be directed to certain tests used when the suspicion exists that the ocular tension may be too high—i.e., when the possibility of glaucoma exists.

PRINCIPLES OF TESTS OF ORGAN FUNCTION.

General Considerations.

Organ function tests, in general, are of two main types—(*a*) tests of normal organ or tissue function, both qualitative and quantitative, and (*b*) tests of the functional reserve capacity.

In this latter type of test, a strain or load in excess of normal physiological limits is imposed upon the organ, and the ability of the latter to function under such extreme conditions is examined and measured.

The functional reserve capacity is influenced by the following four types of factors: (i) Structural factors: (*a*) normal morphology, (*b*) morphological variations, within normal limits morphologically, but perhaps not so functionally, and (*c*) structural variations due to pathological processes. (ii) Physiological factors: (*a*) functional variations dependent on (i) (*b*) and (i) (*c*), and (*b*) variations in the physiological controlling mechanisms, both neural and chemical. (iii) Pharmacological factors—i.e., the effect of drugs administered locally or generally. (iv) Technical factors—i.e., problems of laboratory or clinical techniques of testing and measurement.

The importance of tests of functional reserve capacity of organs lies in their use in detecting early departures from the usually accepted limits of normal physiological function: thus, early pathological processes may be demonstrated before morphological changes become apparent.

Special Considerations.

When the foregoing general considerations are applied to the eye with proven or suspected glaucoma, it becomes apparent that there are two main groups of relevant organ function tests—(*a*) those of the retina and optic nerve, and (*b*) those of the ocular tension, and the mixed group of anatomical and physiological factors determining this.

Retinal function and optic nerve function are examined and tested by estimation of the visual acuity, by examination of the dark adaptation process, and by qualitative and quantitative studies of the entire visual field.

Organ function tests relevant to the ocular tension are more complex, and are dependent on many known, and some unknown, anatomical and physiological factors, most of which vary in terms both of space and of time. Hence, the measurement of normally occurring ocular tension is fraught with difficulties and problems. The estimation of the functional reserve capacity of the eye with relationship to ocular tension constitutes the essence of provocative tests for glaucoma, and because of the several factors mentioned, the application and interpretation of provocative tests for glaucoma abound with difficulties and uncertainties. For similar reasons, the reliability of any one test is not, by comparison, very great. Essentially, we are endeavouring to estimate the functional reserve capacity of several tissues, coordinated in an as yet incompletely understood fashion, and controlled by an equally incompletely comprehended mechanism or group of mechanisms. The ideal provocative test is one which tests the functional reserve capacity of one component of the ocular tension determining mechanism.

Provocative tests may be used for (*a*) the diagnosis of early glaucoma, (*b*) the assessment of glaucoma therapy, both medical and surgical, and (*c*) the diagnosis of the preglaucomatous phase.

The preglaucomatous phase exists in an eye in which the ocular tension is within normal limits over the 24-hour period, but the functional reserve capacity of the eye is impaired, so that provocative tests cause an abnormal rise in ocular tension, indicating interference with the normally coordinated physiological mechanism determining ocular tension. Certain structural abnormalities may exist and arouse suspicion of the preglaumatous phase; examples are the shallow anterior chamber with closed-angle glaucoma, and early peripheral rubeosis iridis in diabetic glaucoma. However, in most cases of preglaucoma there are no tell-tale suggestive morphological variations, and in these cases this preglaucomatous phase is unrecognized; the important example of this is, of course, chronic simple glaucoma.

PROVOCATIVE TESTS FOR GLAUCOMA.

The aim of provocative tests for glaucoma is to reveal instability of ocular tension, even at normotensive levels, as this is the earliest sign of the disease. This may be detected by observations of the phasic diurnal variation in ocular tension; in addition, special tests for estimating the facility of aqueous outflow from the anterior chamber have been devised. Thus, there are three groups of observations which can be made in assessing the functional capacity of the ocular tension mechanism; these are: (*a*) estimation of the phasic diurnal variation in ocular tension, (*b*) aqueous outflow studies and (*c*) provocative tests proper. Each of these will now be considered.

[1] Read at a meeting of the Clinical Society of the Victorian Eye and Ear Hospital, Melbourne, on August 4, 1958.

Phasic Variation of Ocular Tension.

The existence of a diurnal phasic variation of ocular tension has been known for many years (Maslenikow, 1904), but it appears that only in the past decade or so has much use of this knowledge been made in the early diagnosis of glaucoma. The normal variation is 3 or 4 mm. of mercury (Schiotz), with the maximum tension usually occurring between 5 a.m. and 8 a.m. If the variation of tension over the 24-hour period is greater than 5 mm. of mercury (Schiotz), glaucoma exists (Langley and Swanljung, 1951).

"Phasing" is probably the most reliable and profitable investigation in the diagnosis of glaucoma; hourly or two-hourly measurements of tension are made for 24 hours at least. This requires hospital beds and suitably trained nurses or technicians, and these factors, obviously, prevent a much more extensive use of this test.

In the Glaucoma Research Unit there are two techniques for phasing: (*a*) "the full routine" (comparable with the stabilization of a diabetic) in which the patient is admitted for two days over a week-end and the tension is observed as described above, without the use of miotics for the first 24 hours, and with the use of an appropriate miotic for the second 24 hours; (*b*) "the modified phasing routine", in which the ocular tension is measured two-hourly between 9 a.m. and 5 p.m. on one, two, or more days, according to the circumstances of the patient. This method is, of course, not new, and has been used by many oculists for a long time. We find that not infrequently the full routine must be resorted to even after modified phasing, although this method has quite firmly established itself as a worthwhile procedure.

There are no limiting indications, and any eye can be phased. Complications are infrequent, but the following have been encountered: (i) Conjunctivitis and corneal abrasions due to the mechanical effect of the tonometer and the effect of the local anæsthetic drops. Methyl cellulose eyedrops or an oily drop should be instilled after each application of the tonometer. (ii) Hyphæma. This has been encountered once in an eye with thrombotic glaucoma and new vessel formation in the iris. (iii) Acute congestive glaucoma. This has been precipitated in both eyes of a woman with narrow open angles, who also gave a strongly positive response to the water-drinking test.

Aqueous Outflow Studies.

Aqueous outflow studies are designed to assess the functional efficiency of the drainage mechanism from the anterior chamber. A known force is applied to the eye for a known period of time, and the change in tension over this period is measured. From these observations a numerical representation of the facility of aqueous outflow from the anterior chamber can be calculated. This forms the basis of the bulbar pressure test and of tonography.

Bulbar Pressure Test.

The bulbar pressure test was introduced by Blaxter in 1953, and is performed as follows: the Schiotz-X tonometer is applied to the cornea and reading A is taken. With a Bailliart's ophthalmo-dynamometer, 50 grammes' pressure is applied over the insertion of the lateral rectus muscle, with the tonometer still in place—i.e., 65 grammes' pressure is applied; after a delay of 10 to 15 seconds to allow the intraocular pressure to become stable, reading B is taken. This pressure of 65 grammes is maintained for four minutes and then reading C is taken. The dynamometer is removed and reading D is taken immediately. From this, the "outflow fraction" (O.F.) may be calculated as follows:

$$O.F. = \frac{(B - C)\ 100}{B}$$

The normal eye has an outflow fraction of 30% or more. This test can be applied only to eyes with wide anterior chamber angles.

Practical details include: the use of a self-retaining speculum to separate the lids and also to lift them off the globe; the instillation of an eyedrop throughout the test to keep both cornea moist—i.e., mercury oxycyanide, 1 in 10,000; and the instillation of an oily drop after the test—e.g., sodium sulphacetamide (10%) in cod-liver oil. "Decicain" (0·5% solution) is used for local anæsthesia.

The test is of greatest value in early cases of simple glaucoma, and Blaxter's figures are very impressive. Our own experience has been that in cases of wide-angle glaucoma with significant phasic variation of ocular tension, a positive result is always obtained with the bulbar pressure test. When phasing has not been possible—in most cases when the outflow fraction is less than 30%—there is other evidence of a confirmatory nature of preglaucoma or manifest glaucoma. The test appears to be quite reliable, simple to perform, and of significant diagnostic and prognostic value.

Tonography.

The historical development of tonography and ocular massage tests is well considered in Sugar's book "The Glaucomas". From this it appears that in 1878 Pagenstecher first pointed out that massage of the eyeball was followed by a lowering of ocular tension. Various studies along similar lines were carried out, with improved methods, extension of principles and numerical consideration of observations. Eventually, in 1950, emerged Morton Grant's application of the electronic tonometer to the problem, with the evolution of the concept of the "coefficient of facility of aqueous outflow", and modern tonography (Grant, 1950; Sugar, 1957).

Sugar (1957) defines tonography as a procedure in which the drop in ocular tension is observed continuously while an electronic Schiotz tonometer is applied to the anæsthetized cornea continuously for four to six minutes. A recording galvanometer is used to record the findings graphically. The ease with which aqueous may leave the eye is expressed in terms of the coefficient of outflow facility, C—that is, outflow in cubic millimetres per minute per millimetre of mercury pressure gradient—or in terms of coefficient of resistance, R.

A modified form of the originally defined method of tonography may be carried out by the use of a mechanical tonometer, such as the standard Schiotz tonometer. This is probably less accurate, but serves a useful purpose in diagnosis, provided that the limitations of the method are realized. We use this technique for estimating aqueous outflow in eyes which have not a wide angle; we attach less significance to the results than we do to those for the bulbar pressure test. Several series of tables have been published for mechanical tonography by Ballantine (1954), Sugar (1957) and others, and reference should be made to these authors.

Provocative Tests.

For each of the provocative tests, of which there are many, numerous series of observations have been published, so that we now know (*a*) the results which are within the physiological range of normality, (*b*) the results which are of pathological significance, (*c*) the error of each method, (*d*) the general degree of reliability of each test, and (*e*) the indications for the application of each test.

Less certain are we of the mechanism of most of the tests, although the postulated mechanisms, considered together, cover most of the recognized variable factors concerned in the maintenance of ocular tension.

Certain problems and difficulties are presented in applying provocative tests for glaucoma. These include: (i) the existence of many factors and controlling influences concerned with the maintenance of normal intraocular pressure; (ii) the existence of a diurnal phasic variation in intraocular pressure; (iii) the fact that in many cases of glaucoma, more than one ætiological factor is involved; (iv) certain technical problems.

The outstanding consideration here is the question of standardization of tonometers, to which subject I have devoted much study and thought; and I have been able to arrange for the generous donation of equipment and technical services, so that a tonometer testing station has been established at the Glaucoma Research Unit of the Victorian Eye and Ear Hospital.[1]

Sir Thomas Lewis has written: "It is crucial in measuring to know the error of the method: to have but an inaccurate measure may be regrettable but to have it and not to know it is deplorable." Surely, no more need be said about the desirability of routine tonometer testing or, for that matter, of the testing of all other instruments used in clinical mensuration.

Consideration of the necessity of gonioscopy in order to select the appropriate provocative test leads to a useful clinical classification of provocative tests, as follows:

Eyes with a narrow angle anterior chamber: (i) darkroom test; (ii) mydriatic test; (iii) reading test; (iv) tonography.

Eyes with a wide angle anterior chamber: (i) bulbar pressure test; (ii) tonography.

Eyes with narrow or wide angle anterior chambers: (i) water-drinking test; (ii) tonography; (iii) "Priscoline" test; (iv) fluorometry (Goldmann).

There are many other tests; but I propose only to say a few words about the tests we regularly use at the Glaucoma Research Unit of the Victorian Eye and Ear Hospital. With all tonometric methods we record certain basic data—viz., the number and type of tonometer used, the time of tonometry or provocative test, the time of administration of the last eyedrops or tablet ("Diamox" or "Cardrase") and the nature and dosage of both of the latter.

Water-Drinking Test (Schmidt, 1928).

In this test, after tonometry the patient drinks 1000 ml. of water and the tension is measured half-hourly for two hours. A rise of 8 mm. of mercury (Schiotz) is probably abnormal, and a rise of 10 mm. of mercury is definitely abnormal. This is a useful screening all-purpose glaucoma test, but a negative result does not exclude the diagnosis. The test is easily performed, and a positive, or suggestive, result is of great significance. The higher the initial tension, the more likely the results are to be of significance.

Mydriatic Test (Gronholm, 1910).

Tonometry is carried out before and after dilatation of the pupil with homatropine or homatropine and cocaine. A rise of 8 or 9 mm. of mercury (Schiotz) is probably abnormal, and a rise of 12 mm. of mercury is definitely abnormal. Most positive results are obtained with narrow-angle eyes.

This test is probably done more often by more oculists than most realize, and a tension above normal with a dilated pupil must cause a provisional diagnosis of glaucoma or preglaucoma to be made, until the condition is proved otherwise. It has been my impression that this test is often significant with wide-angle as well as narrow-angle eyes, and it is interesting to note that Leydhecher (1955) makes the same observation. This, of course, makes hypotheses with regard to the mechanism of the test more difficult to formulate.

"Priscol" Test (Leydhecker, 1954).

After tonometry, a cotton-wool applicator dipped in local anæsthetic is placed against the bulbar conjunctiva at the 12 o'clock position, with the patient looking down and the upper eyelid retracted. After one minute, 1 ml. of "Priscol" is injected subconjunctivally. The tension is measured after 15, 30, 60 and 90 minutes. A rise of 11 to 13 mm. of mercury (Schiotz) is probably abnormal, and a rise of 14 mm. definitely abnormal.

[1] The results obtained at this station are most interesting and will be the subject of a further communication.

My experience of this test is very limited. It is rather a severe test, both for the eye and for the patient. Our patients are usually admitted to the unit for phasing before this is undertaken. The percentage of significant results quoted by Leydhecker, who devised the test, is impressive, and there seems to be no doubt of its value.

Darkroom Test (Gronholm, 1910).

Tonometry is carried out, and followed by one hour in complete darkness; the tension is then measured again. Higgitt (1954) states that a rise of 10 mm. of mercury (Schiotz) is abnormal.

Leydhecker (1955) is of the opinion that the darkroom test is less reliable than the mydriatic test, and my clinical impression is in agreement with this. We have obtained very few significant results with this test.

Reading Test (Gradle, 1931).

Tonometry is followed by 30 minutes' concentrated reading; tonometry is then repeated (Gradle, 1931; Miller, 1953; Higgitt and Smith, 1955). Duke-Elder (1957) quotes two cases in which a rise of about 40 mm. of mercury occurred. A further six cases have apparently been found.

I have tried several patients with narrow-angle glaucoma with this test, without significant result. Apparently a mydriatic prevents this rise of tension, and a structural abnormality of the iris or ciliary body, combined with a narrow angle, would appear to be the explanation of this odd phenomenon.

Conclusion.

Two outstanding points have emerged from a study of provocative tests for glaucoma, and it seems desirable to mention these again: first, the necessity of performing gonioscopy before carrying out any provocative test; and secondly, the fact that "phasing" is of paramount importance and must always constitute the last court of appeal in cases of doubt.

In conclusion, I would emphasize what is well known to all, that the diagnosis of glaucoma depends on much more than tonometry and its various offshoots, and would stress that, at the Glaucoma Research Unit, in spite of any ideas you may have formed as a result of tonight's discussion, in the management of glaucoma we are not overtly over-awed by outflow or shamelessly shackled to a Schiotz.

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THE ANTI-HUMAN-GLOBULIN-INHIBITION TEST. A SIMPLIFIED TECHNIQUE.

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THE following article is a brief description of the principles and technique of the anti-human-globulin-inhibition test as carried out in the medico-legal section of the Department of Public Health, New South Wales. The purpose of the test is to demonstrate the human origin of blood stains and pieces of tissue, particularly in forensic medicine. It is not intended to present this article as being the result of original work, but it is considered that the method described below is in some respects an improvement on methods already suggested in that it is applicable to the small amounts of blood stain often found on material submitted by the police for examination.

In examining blood stains for medico-legal purposes, one of the essential tests concerns the identification of the species source of the blood. For many years it has been routine to employ the precipitin test for this purpose. This test, although very useful, has certain disadvantages. It involves the use of antisera, which must be highly specific for the animal species for which the blood is being tested. The reagents involved in the test must be absolutely clear, a requirement which cannot always be met. Thus there is doubt at times concerning the interpretation of the test.

After the publication of an article by Coombs, Mourant and Race in 1945, in which they described the method of preparation of antiglobulin serum, Allison and Morton (1953) described the inhibition of antiglobulin sera by blood stains. The inhibition was found to be specific for the species of blood concerned, and a method was recommended by which the species of origin of blood stains might be identified with the use of antiglobulin serum.

In 1954 Anderson described similar investigations and suggested two possible techniques for the same test in which extracts of blood stains of unknown origin are allowed to incubate with antiglobulin serum, after which it is tested for its ability to agglutinate sensitized cells. For full details the reader is referred to the original articles.

After the publication of the above-mentioned articles trials of the method were carried out in the medico-legal section of the Department of Public Health, and finally a simple and reliable technique was evolved for the identification of human blood stains, which could be applied to the minute quantities of stain often encountered on material submitted by the police for examination. This method has now been in use in this department for more than three years, and has been employed in the investigation of at least 60 cases of violent crime. At least 170 separate tests have been performed to prove the human origin of blood stains or tissue. In cases which gave a negative reaction a precipitin reaction was also carried out to confirm that the blood was of non-human origin.

The advantages of the anti-human-globulin-inhibition test over the precipitin test are as follows: (i) The result is clear cut, i.e., there is either definite agglutination of the cells or absence of agglutination. (ii) The amount of material required is very minute. A clear-cut result can be obtained with the use of a spot of blood one-twelfth of an inch in diameter or less on fine linen, an amount which would be quite useless for a precipitin test. (iii) The test can be applied not only to blood stains but also to fragments of tissue by virtue of the small amount of serum found in the tissue. (iv) The anti-human-globulin element in the serum is so specific that the presence of non-specific elements such as that giving a general mammalian reaction is of no importance, and there is no need to subject the serum to absorption to remove non-specific elements. For this reason anti-globulin sera of very high titre can be prepared.

Principle of the Test.

Group O Rh-positive human red blood corpuscles which have been sensitized with incomplete anti-D serum are normally agglutinated by anti-human-globulin serum. If, however, the anti-human-globulin serum is first incubated with human blood serum, or human tissue containing some serum, the ability to agglutinate the sensitized corpuscles is inhibited. Serum from any other animal has no such property of inhibiting the anti-human-globulin serum with the exception of chimpanzee serum.

Materials Required.

1, Anti-human-globulin serum (Coombs serum). The serum used in this department is made on the spot by immunizing rabbits with alum-precipitated human serum intramuscularly, followed by intraperitoneal and intravenous injections of sterile human serum over a period of some weeks. The antiserum so produced has a very high titre. The optimum strength of the anti-human-globulin serum for the agglutination reaction is 1 in 80. With this fact in mind, the serum for routine use is diluted in the first instance 1 in 5 in saline solution and made up into ampoules for storage in the refrigerator. It keeps well, and after three years we have been unable to detect any apparent deterioration of our stock.

2. Anti-D serum. A strong anti-D serum is used. The serum employed in this laboratory is obtained by courtesy of the Red Cross Blood Transfusion Service.

3. Group O Rh-positive human red blood corpuscles. Fresh corpuscles should always be used. Deterioration of the Rh factor takes place fairly rapidly. In this laboratory clots remaining after separation of the current day's specimens of blood for Wassermann test, or a known donor are used.

4. Controls. These are blood stains of known human blood and of non-human blood. They are prepared by the appropriate bloods (human, dog, ox, etc.) being dropped on filter paper and allowed to dry.

5. Blood stains to be tested. In this department the stains to be tested are found on articles submitted by the police such as clothing, weapons, etc. The amount of stain required to produce a clear-cut result is very minute and is that amount which will produce a faint coloration in two small drops of diluted antiserum. In the case of fragments of tissue, no pink coloration may be visible and the amount of tissue employed must be judged from experience. A clear-cut result has been obtained with a shred of skin one-twelfth of an inch square and less than one millimetre thick.

Technique of the Test.

Preparation of Sensitized Cells.

A fairly thick suspension of group O Rh-positive human red blood corpuscles is made in six or seven drops of strong incomplete anti-D serum in a centrifuge tube. The suspension is incubated at 37° C. for one hour, after which the cells are washed four times in saline solution, each time filling the centrifuge tube. Thorough washing of the cells is most essential, as any trace of serum left behind will tend to prevent agglutination in the controls. Finally, the suspension is made up to about 4%.

Preliminary Dilution of Anti-Human-Globulin Serum.

Stock Coombs serum (1 in 5) is diluted 1 in 8 to produce a final dilution of 1 in 40. A sufficient quantity is prepared to allow two drops for each tube of the tests and controls. The test is set up as follows, in glass tubes measuring three inches by three-eighths of an inch (Kahn tubes).

	Controls			Stain A		Stain B	
0	0	0	0	0	0	0	0
1	2	3	4	Test	Control	Test	Control

Four general controls are used as well as an extra control for each stain, in which the blood is in the form of stain on material. If flakes of dried blood are used without any other material, then no extra control is required.

To each tube of the tests and controls two drops of the 1 in 40 anti-human-globulin serum is added, with the use of a dropper delivering 0·015 ml. per drop.

To the control tubes and tubes of the tests blood stains are added as follows.

First Control: filter paper containing non-human blood stain (e.g., ox blood) one-twelfth of an inch square.

Second Control: filter paper containing some other non-human blood stain (e.g., dog's blood) one-twelfth of an inch square.

Third Control: filter paper containing known human blood stain one-twelfth of an inch square.

Fourth Control: no blood stain to be added.

Test A: material containing stain A to be tested, one-twelfth of an inch square; or sufficient flakes of dried blood to impart a faint coloration to the anti-human-globulin serum; or a small fragment of tissue to be tested.

Control A: only to be used if the blood is in the form of a stain upon material; a piece of unstained material one-twelfth of an inch square from the garment from which the stain was taken for Test A.

Test B, Control B, etc.: same as Test A and Test B, etc., using different stains.

The stain in the tubes is in each case mixed intimately with the anti-human-globulin serum by using small glass rods, pressing and squeezing the blotting paper or material containing the stain until it is all in solution.

Each tube is corked and incubated for one hour at 37° C.

At the end of one hour two drops of a well-washed suspension of sensitized human red blood cells are added to each tube, which is shaken, recorked and incubated for one hour at 37° C.

At the end of the second hour each tube is spun in the centrifuge at 1500 r.p.m. for one minute. The cells are resuspended in each tube by the tube being rotated a few times between the hands to break up the button of cells at the bottom of the tube.

The liquid in each tube is turned onto a microscope slide and examined microscopically for agglutination. The result should be clear cut, i.e., the agglutination is either marked or absent. Agglutination occurs in all tubes in which there is no human blood or tissue. Absence of agglutination occurs in the tube in which there is known human blood stain.

Assuming the controls to be in order, then absence of agglutination in tubes A, B, etc., indicates that the stain or tissue as the case may be is of human origin.

Discussion.

At the time of writing, 170 anti-human-globulin-inhibition tests had been carried out. Of these 152 blood stains gave a positive result, indicating that the stains were of human origin. Six tests involved fragments of tissue (skin) found either on motor-cars in hit-run cases or on weapons. In four of these a positive result was given for human origin. In the remaining two the amount of tissue was so tiny that no inhibition took place, and the origin of the tissue could not be demonstrated. In four cases the result of the test was unsatisfactory as the cells became hæmolysed. In one of these four cases the stain was on a towel, and traces of soap were probably responsible for the hæmolysis. Other factors, such as traces of urine, dyes, etc., are thought to be causes of hæmolysis of the cells. In the case of dyed material it was found that hæmolysis might be prevented by removal of the fragment of material holding the stain after the blood was expressed and before the first incubation.

Summary.

A method is described for the demonstration of the human origin of blood stains and tissues, which has been in use for more than three years in the medico-legal section of the Department of Public Health, and which has proved satisfactory in practice.

Acknowledgements.

I wish to record my appreciation of the helpful advice given by Dr. Farquhar Fraser, Director of Pathological Laboratories, at whose suggestion this work was first undertaken, and to Dr. H. G. Wallace, Director-General of Public Health, for permission to publish this article.

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MENOPHANIA AND REGULARITY OF MENSTRUATION.

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THE medical records of all girls who were pupils at a girls' private school in Melbourne between the years 1935 and 1956, were analysed to determine the age of onset of menstruation and the age at which the menstrual period became regular.

TABLE I.
Age at which Menstruation Commenced and its Regularity.

Age. (Years.)	Regularity.		Total.	Percentage of Total.
	Regular when at School.	Not Regular when at School.		
10	6	1	7	0·8
11	62	5	67	8·0
12	177	17	194	23·0
13	254	31	285	34·0
14	162	42	204	24·0
15	48	18	66	8·0
16	7	3	10	1·0
17	—	—	—	—
18	—	2	2	0·2
Total	716	119	835	—

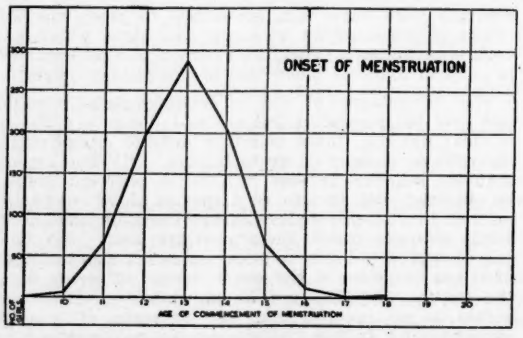

FIGURE I.

These girls were medically examined each year by the school doctor, and information regarding menstruation

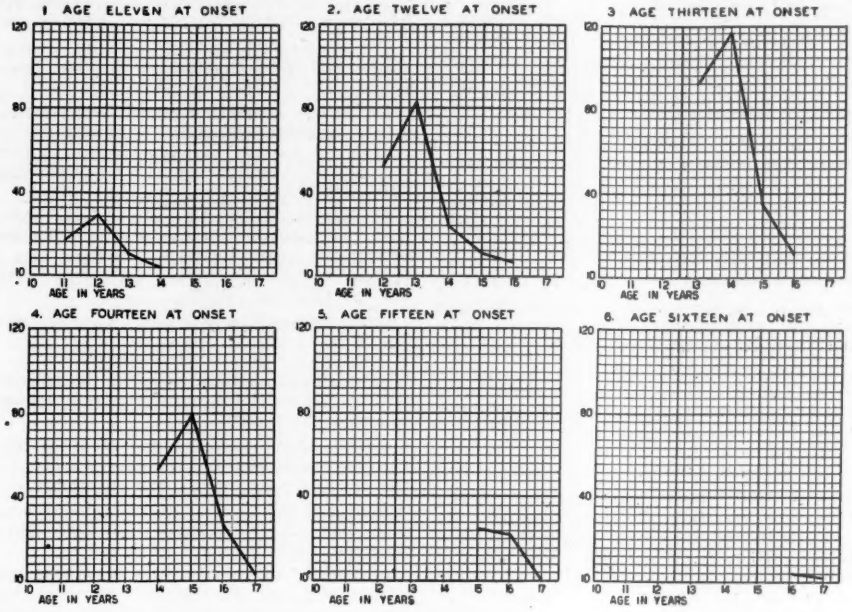

FIGURE II.

was collected at the medical examination. Of the 921 medical records examined, in 86 the information was incomplete so these have been excluded from the study.

The results are expressed in Tables I and II and in Figures I, II and III. The figures obtained regarding the age of onset of menstruation, when plotted, give a normal distribution curve with the mode at 13 years (see Figure I).

TABLE II.

Percentage of Girls Developing Regularity of Menstruation each Year after Onset

Age of commencement of menstruation	Age at which menstruation became regular: 10	11	12	13	14	15	16	17	18	Total
10	1	1	1	1	1	1				6
11	—	17	29	11	5					62
12	—	—	53	82	24	11	7			177
13	—	—	—	92	116	35	11			254
14	—	—	—	—	53	80	26	3		162
15	—	—	—	—	—	25	22	1		48
16	—	—	—	—	—	—	4	2	1	7
Total	1	18	83	186	199	152	70	6	1	716

1st year 34%
2nd year 46%
3rd year 14%
4th year 4%

In the majority of cases menstruation became regular in the second year after the onset of menstruation, but in 119 girls (14·3%) menstruation had not become regular by the time they had left school.

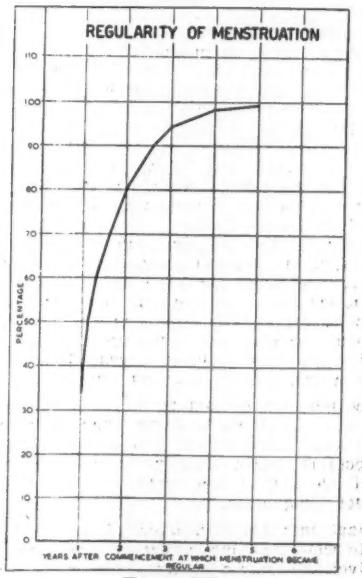

FIGURE III.

Reports of Cases.

AN ACUTE HALLUCINATORY EPISODE WITH RECOVERY.

By E. FISCHER,[1]
Sydney.

HALLUCINATIONS are sensory impressions without external stimulation. There is no outward source for the imagined voices, visions, odours, tastes or tactile sensations.

[1] Formerly Superintendent, Admission Centre, Darlinghurst, N.S.W.

Most frequently delirious reactions of an infectious or toxic origin give rise to hallucinations, visual hallucinations being more frequent than auditory ones. Schizophrenic children often have hallucinations, auditory and visual hallucinations being reported most frequently. The child's attitude to them is usually one of indifference; occasionally they fit in with the delusional contents or are elaborated by the child in a delusional manner.

Organic lesions of the brain may give rise to hallucinations. Their nature depends on the specific location of the cerebral lesion, e.g., olfactory in lesions of the uncinate gyrus, visual in tumours of the occipital lobe. In other cases there seems to be no connexion between the type of sensory deception and the anatomical site of tissue destruction—e.g., in encephalitis or in juvenile paresis.

Hallucinations occur sometimes in epileptic children and in hysterical and migrainous twilight states. They are often noticed in post-infectious psychoses.

A case of an acute hallucinatory episode with complete recovery in twelve hours without apparent cause in a child aged seven years does not appear in the literature. The case presented here will therefore be of interest.

Clinical Record.

The patient, aged seven years, was admitted to the Admission Centre, Darlinghurst, at about 10 p.m. on December 24, 1958, with the following history (obtained from his general practitioner). "The child, who lives in a foster home, was seen by his parents last week. For the past few days he has become non-cooperative and talking about his mother. At present he is irritable and restless and impossible to control. Thank you for admitting him."

On admission to hospital, the child was acutely excited and appeared very apprehensive. He was shouting: "Don't let them touch me!" and "Go away, Vincent". He was dashing up and down the room and hitting out with his hands at everything and anyone within his reach. He was pointing at the ceiling, saying, "They are up there", and when asked "Who is up there?", he said, "Little things", but would not elaborate further. He was threading an imaginary needle, he performed all sorts of imaginary actions and movements, and he dashed into the wall as if it did not exist. He was obviously grossly hallucinated; in fact, his condition was so similar to that seen in delirium tremens that it was thought that he might have had some alcoholic drink (particularly as it was Christmas Eve). On inquiry this was excluded. With the exception of a few scratches on his legs, physical examination revealed no abnormality; his temperature was 98·4° F. and his pulse rate was 86 per minute. His heart, lungs and central nervous system were normal.

He received three-quarters of a grain of "Sodium Amytal" with no effect, and one hour later he was given one-third of a millilitre of "Sodium Gardenal" solution intramuscularly again without effect. Finally he fell asleep at 4.50 a.m. in the arms of the nurse, in a state of complete exhaustion.

The next morning, December 25, at 8 a.m., the child was quite well—his temperature at that time was 100° F.; he received an aspirin tablet, and by 12 noon he was absolutely normal, both physically and mentally. There was no trace of any hallucinations or of any other mental abnormality He was playing with toys and gave a coherent and good account of himself. He had complete amnesia of the whole episode.

The foster parents were interviewed, and they gave the following story. He had been with them for about ten months, during which time he had been well behaved and a likeable child, taking part in play with other children, and he had good reports at school. Some ten days prior to the above-mentioned episode the child went to see his parents, and a few days after they noticed that "he was not the same"—but they could not give any details. On the evening of December 24 he became disturbed and was talking nonsense. He said: "I can't have my tea, don't tie a string around the baby's neck." He became very restless, and they called the doctor, who sent him into the Admission Centre. On his way here he vomited a little.

His normal state continued; on December 29 he was discharged from hospital and he has remained well ever since.

He is one of eight children. His father is a labourer whose earnings are erratic. He was a heavy drinker, but in 1957 he is said to have modified his drinking habits. His mother is rather dull, but is described as a "reasonably nice woman".

In 1957 the child was removed from his parents together with the other children, and the parents were convicted of being incapable of caring for them and, as stated above, the patient has been living with his present foster parents for the past ten months.

His previous illnesses had been measles and mumps.

Discussion.

Acute hallucinatory episodes with complete recovery within twelve hours or so do not appear to have been reported previously.

Levin (1932) reported the cases of four non-psychotic children with auditory hallucinations who were between the ages of seven and fourteen years.

Sherman and Beverly (1924) gave an account of children who had hallucinations who were below the age of fourteen years.

It should be noted that in both the above-mentioned series, totalling 23 children, the hallucinations were of long standing, as well as entirely different in character and in reaction to the case presented here. The authors could trace the hallucinations through several stages of development. A boy who saw God on the one side and the Devil on the other first argued with himself about being good, then recognized vague images, one saying "Be good", the other "Be bad". They also pointed out that, in contrast to the hallucinations of adults, those experienced by children are comparatively simple and much less removed from the environmental situations in which they developed.

In the present case, the hallucinations were far from simple, and they appeared to have been triggered off from the child's visit to his parents, some ten days previously, during which time the child expressed fear of being returned to them, culminating with the acute manifestations described above, and ultimately making a complete recovery within the short period of twelve hours.

Acknowledgements.

I wish to express my very sincere thanks to Dr. Donald S. Fraser, Inspector-General of Mental Hospitals for N.S.W., for his kind permission to publish this case; to Dr. Elizabeth Linklater for her observations of the case; and to Miss M. Mills, psychiatric social worker, for her efforts in obtaining the family history and follow-up.

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ACUTE HEMIPLEGIA COMPLICATING CARDIAC DISEASE IN CHILDREN.

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THE occurrence of acute hemiplegia in children suffering from cardiac disease has been reported by Leech (1935).

Ford (1937) listed two cases of congenital heart disease and hemiplegia, and described the autopsy findings in

each. He attributed the condition to cerebral thrombosis due to secondary polycythæmia.

Wood (1942) described a case of congenital pulmonary stenosis and atrial septal defect, complicated by spastic paresis of both legs and the left arm. At the post-mortem examination, the cerebral changes found consisted of severe congestion without infarction.

Later in the same year, Corner and Perry (1942) reported three such cases of cyanotic heart disease, but noted that one child had a hemoglobin value of 90%. They concluded that, in the absence of either emboli or subacute endocarditis, the ætiology was obscure.

An interesting case of a girl with Fallot's tetralogy was discussed by Fischer and Florman (1943). This girl had suffered right hemiplegia at the age of eight years. After three months no residual signs remained, but two years later she developed diabetes mellitus. One year later, in a hypoglycæmic coma, she showed signs of right hemiplegia, which disappeared in five days as her diabetic state became controlled.

Gross (1945), in discussing arterial embolism and thrombosis in children, incriminated congenital heart disease as one cause, and stated that embolism in such cases almost certainly carried a fatal prognosis.

More recently, Tyler (1957) described the incidence of neurological disorders in congenital heart disease. Of a total of 1875 patients, 72 (3·8%) had cerebrovascular accidents, the highest incidence being in cases of Ebstein's malformation, transposition of the great vessels, pure pulmonary stenosis and Fallot's tetralogy. Of 1684 patients, 1·6% had cerebral abscesses. With one exception, all were patients with cyanotic heart disease.

Five additional cases of congenital heart disease complicated by hemiparesis are now reported briefly.

Clinical Records.

Case I.—A male patient, aged one year, was known to have a congenital heart lesion with persistent central cyanosis. He was admitted to hospital because of an inability to use his right arm on the preceding night. On the morning of his admission he had kicked his right leg and rolled his eyes for a few seconds. Examination showed him to be a cyanotic boy with signs suggestive of Fallot's tetralogy. He had right hemiparesis; sensation was intact. Carotid pulsations were present, and no cephalic bruit was heard. His hemiparesis diminished over a month, and he was discharged from hospital. His hæmoglobin value on five occasions ranged from 62% (9·3 grammes per 100 ml.) to 78% (11·7 grammes per 100 ml.).

Case II.—A male patient, aged two years, had been cyanotic since birth. On three occasions during the preceding nine months he had suffered from loss of power in his right arm and the right side of his face, the right leg also being affected in the second attack. When examined he showed signs of Fallot's tetralogy and right hemiparesis. The latter did not decrease over his five weeks' period in hospital. His hæmoglobin value was 114% (17 grammes per 100 ml.).

Case III.—A male patient, aged two years, presented at this hospital with the story that he had suddenly become very ill after a "cold" the preceding week. Examination showed him to be cyanotic, desperately ill and semicomatose, with the clinical signs of Fallot's tetralogy and left hemiplegia. He died in 12 hours.

Post-mortem examination revealed a right frontal abscess that had ruptured into the right lateral ventricle of the brain.

Case IV.—A male patient, aged six years, had been well until, after an upper respiratory tract infection, he began dribbling out of the left side of his mouth and fell to the left when he walked. On examination, he was found to have left hemiparesis, hypertension and absence of femoral pulses. A diastolic murmur was heard for the first time two weeks after his admission to hospital, and his spleen was palpable. Intensive investigations failed to produce any supportive evidence of subacute bacterial endocarditis, and viral studies on the fæces and cerebro-spinal fluid gave negative results. With no specific therapy he improved, regaining the use of his left leg more quickly than the use of his hand. Operation four months later revealed a coarctation of the aorta; no vegetations were seen in relation to the coarctation. He has remained well, with only slight weakness of the arm and leg.

Case V.—A female patient, aged 15 months, presented in congestive cardiac failure after an influenza-like illness one month previously. X-ray examination of the chest revealed non-specific cardiac enlargement, and the electrocardiographic changes were consistent with myocarditis. She improved with digoxin and diuretic therapy. Two weeks later, however, her face was noted to be asymmetrical, and weakness of the right arm and leg was present. Lumbar puncture furnished normal cerebrospinal fluid, and no virus was grown from it. The hemiparesis decreased, and she was discharged from hospital after one month.

Twelve months later she was readmitted, with persisting slight weakness of her right arm and leg, and a large, quiet heart, with no signs of congestive failure. The electrocardiogram now showed left ventricular hypertrophy and strain. After a respiratory tract infection, however, she again developed congestive cardiac failure and required further treatment with digitalis. This was ceased before her discharge from hospital. She could walk well, with only slight dragging of her right foot, and her mental ability was normal for her age. Fibroelastosis was considered as a diagnosis; but the relatively benign course over the 12 months following the first admission to hospital would tend to rule this out.

Discussion.

Of the three cases of Fallot's tetralogy, one (Case III) provided autopsy evidence. This consisted of classical Fallot's tetralogy and an abscess of the right frontal lobe of the brain. This association is not uncommon in cyanotic heart disease.

In the other two cases of Fallot's tetralogy, arterial thrombosis secondary to hæmoconcentration is considered unlikely. In Case I the hæmoglobin value was only 11·7 grammes per 100 ml., and although in Case II a reading of 17 grammes per 100 ml. was obtained, we have frequently encountered high values in cases of Fallot's tetralogy in which there was no evidence of intravascular thrombosis. Alternative possibilities are: (i) atheroma of the cerebral arteries; (ii) arterial embolus; (iii) congenital lesions such as arterio-venous malformations or aneurysms. However, this explanation would not account fully for the hemiparesis in Case II. In this instance we may postulate that anoxia plays an important role in producing hemiparesis in cases of cyanotic heart disease. Oxygen deficiency would aggravate any pre-existing lesion, and possibly, according to the anatomical variations of blood-vessel anastomosis, determine areas of reversible (or later irreversible) damage.

In Case IV, the known association of coarctation and cerebral vascular malformation would make this a likely diagnosis, since subacute bacterial endocarditis can be excluded.

Case V presented as myocarditis complicated by hemiparesis. This may have been due to a virus, neurotropic as well as "myotropic". Against this, however, are the late onset of the hemiparesis (six weeks after the onset of the illness), and the failure to isolate the virus from the cerebro-spinal fluid. Alternatively, the condition could be an embolus from a mural thrombus with no further embolization to date.

There is thus probably no single cause for hemiplegia complicating heart disease in children. In the cases in which cyanosis is present, anoxia rather than hæmoconcentration would appear to be the important factor.

Summary.

1. Five cases of cardiac disease with hemiparesis in children are reported.

2. The literature is briefly reviewed.

3. Possible mechanisms are discussed, and the importance of anoxia rather than hæmoconcentration is emphasized.

Acknowledgements.

I wish to thank the physicians who allowed their cases to be presented, Dr. John Sutherland for his advice and interest, and Dr. D. C. Fison, Superintendent of the Brisbane Children's Hospital, for access to hospital records.

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FIVE-YEAR SURVIVAL AFTER RESECTION OF A CARCINOMA OF THE MIDDLE THIRD OF THE ŒSOPHAGUS.

By A. E. M. REDDEL, M.B., M.S., F.R.A.C.S., F.A.C.S.,

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IN October, 1953, Mrs. A., aged 65 years, was admitted under my care at the Western Suburbs Hospital, Sydney, complaining of difficulty in swallowing and pain behind the sternum, which had been present for several months. An X-ray examination by Dr. B. Frecker prior to her admission to hospital had revealed the presence of a lesion strongly suggestive of carcinoma in the middle third of the œsophagus.

An œsophagoscopy was performed by Dr. A. M. Bryson, and a large ulcerating growth was detected, but a fairly good lumen was still present in the œsophagus. A biopsy was taken, and this revealed a well-differentiated squamous carcinoma. Dr. Bryson also performed a bronchoscopy, and no abnormality was detected.

After careful preparation it was decided to resect the growth according to the method of Mr. Ivor Lewis.

The anæsthetic was administered by Dr. Chris. Davidson, and Dr. Russell Roxburgh assisted with the operation. A left paramedian incision was made in the abdomen, and the stomach was mobilized, preserving its blood supply at the lower end. The stomach was completely freed to the œsophageal opening of the diaphragm, and this opening was gently dilated, after which the abdomen was closed.

The patient was then placed on the left side, and a right thoracotomy was performed through the sixth intercostal space. The vena azygos was ligated and the growth mobilized, freeing the œsophagus well clear of the growth above and down to the cardio-œsophageal junction below. The stomach was then gently drawn up into the chest through the opening in the diaphragm. The œsophagus was sectioned at the cardio-œsophageal junction, and the stomach was closed. The proximal portion of the œsophagus about one inch above the growth was anastomosed to the upper portion of the stomach, and the chest was closed with drainage.

The patient's convalescence was uneventful, apart from a slight mental aberration after her discharge from hospital.

Since operation she has had a good appetite with no difficulty in swallowing, and has gained over two stone in weight. For a time she resumed her position as domestic help, but in view of her age has since relinquished this. She now performs normal household duties for herself and her husband.

Five years after operation the patient appears well nourished and healthy, and there is no clinical or radiological evidence of recurrence.

Reviews.

Hodgkin's Disease. By Antonio Rottino, E. P. Benditt *et alii*; "Annals of the New York Academy of Sciences", Volume 73, Art. 1; 1958. New York: The New York Academy of Sciences. 9" x 6", pp. 380, with many illustrations. *Price: $4.50.*

THIS collection of 22 papers is the result of a conference on Hodgkin's disease held and supported conjointly by the New York Academy of Sciences and the Damon Runyon Memorial Fund for Cancer Research in New York. It was held in November, 1957. The idea of the monograph has been to cut across broad areas of the problem of Hodgkin's disease so as not only to include discussions on the ætiological and therapeutic aspects of the disease process itself, but also to project a detailed consideration at a fundamental level of the morphology, physiology and metabolism of the cellular types directly or indirectly implicated in Hodgkin's disease. These elements include the lymphocyte, the reticulum cell, the fibroblast, the mast cell, the macrophage and the eosinophil. At the same time, it was felt that contributions from both academicians and clinicians might serve to cross-fertilize ideas and concepts that could ultimately lead to a better understanding of the disease, with regard both to its causes and to possible avenues of treatment. The papers are grouped under four main headings which deal with the lymphocyte, the reticulum cell, cytology and ætiology, and therapy.

The Central Nervous System and Behaviour: Transactions of the First Conference, February 23, 24, 25 and 26, 1958. *Edited by Mary A. B. Brazier, Ph.D.; 1959.* Sponsored by The Josiah Macy, Jr. Foundation and The National Science Foundation. 9" x 6", pp. 450, with 168 illustrations. Price: $5.25.

THIS volume contains the transactions of the first Conference on the Central Nervous System and Behaviour sponsored by the Josiah Macy Junior Foundation and the National Science Foundation in February, 1958. It is set against the background of Russian neurophysiology. The introductory article takes the form of a pictorial survey covering Russian contributions to an understanding of the central nervous system and behaviour. Four articles deal with the nineteenth century background of the Russian neurophysiologist and then severally with Sechenov, Danilevsky, Wedensky, Ukhtomsky, Pavlov and Bechterev. Then follow an article on post-Pavlovian development in conditioned reflexes and a summing-up of this first section of the conference. The remainder of the volume contains papers on brain stimulation and conditioned reflexes, electroencephalographic studies of conditioned learning and electrical correlates of conditioned learning.

Studies on Fertility: Including Papers Read at the Conference of the Society for the Study of Fertility, London, 1958, being Volume X of the Proceedings of the Society. Edited by R. G. Harrison, M.A., D.M.; 1958. Oxford: Blackwell Scientific Publications. 8½" x 5½", pp. 188, with 4 tables. *Price: 25s. (English).*

THESE studies represent the latest scientific and experimental work in this field. If the papers seem far removed from the daily work of sterility clinics, it must be remembered that they provide a chart to map our future course and a compass to direct our further advances. All too commonly the clinician is "bogged down" in the morass of routine investigations, and this book will be to him not only of great interest, but of inestimable worth in providing glimpses of wider horizons.

Bound up with this work, but at the opposite pole, the most widely discussed subject today is probably the control of fertility by oral therapy. Although it is iconoclastic in its implications, many experiments are confirming this possibility, and indeed such medicaments are already on sale to doctors on the open market. Most apposite, then, is the group of papers here presented on the biological and clinical effects of progestogens. The Oliver Bird Lecture, given by Gregory Pincus of Massachusetts, includes interesting field tests which seem to prove, not only that oral progestins are effective as ovulation inhibitors, but also that after their cessation a rapid return to normal fertility is the rule.

It is very refreshing to find that no less than eight papers are devoted to male fertility. They are divided into two sections, studies on human fertility and studies in the experimental animal. The effect of varicocele on spermatogenesis, as studied by Scott of Glasgow, corresponds with our experience in this country—namely, that it effects motility and count rather than sperm morphology. Interesting comparative experiments show the effect of ischæmia on the testes of young rats, differences in the metabolism of spermatozoa and the results of induced seminal degeneration in rabbits. It must, of course, always be borne in mind that conclusions drawn from other species do not necessarily hold good for the human.

To turn to the female partner, a valuable piece of work has been contributed on uterine retrodisplacement and fertility. Leading gynæcologists in this country would agree that this condition rarely causes sterility or predisposes to abortion. Only after all other factors are excluded should correction be considered for infertility, as distinct from dyspareunia. We would explain some apparent inconsistencies in this paper by that delightful phrase "not statistically significant".

From Manchester Jewish Hospital Clinic comes an unexpected chapter on the relation of naso-pharyngeal infection to infertility. Sixteen cases are presented in detail, in which a clear association between the removal of symptomless naso-pharyngeal sepsis and the onset of pregnancy is evident.

Another aspect touched on is that of the psychological origin of infertility. It is postulated that the equal efficacy of diverse therapies may be explained by the common feature of the personal approach.

Experiments with egg transfer in the mouse and insemination by intraperitoneal injection of various animals are of more theoretical than practical interest at present.

Pleasant to read, printed on good quality paper and well illustrated, these 16 papers are presented as separate but correlated entities under the ægis of the Society for the Study of Fertility, London. In this volume we find portrayed the results of original investigation into the scientific basis and the clinical observation of fertility. It shows the current trends in such research in the fields of biological, medical and veterinary study. It is highly recommended, and is, indeed, an essential book for anyone who claims to be a serious worker in this domain.

Reminiscences and Adventures in Circulation Research. By Carl J. Wiggers, M.D.; 1958. New York and London: Grune & Stratton, Incorporated. 9" × 5¾", pp. 416, with 82 illustrations. Price: $9.75.

THE name Carl J. Wiggers needs no introduction to cardiologists and physiologists, who are grateful for his brilliant contributions to many circulatory problems. This book is divided into two portions; the first is autobiographical and describes the environment to which he reacted. The accounts of his early years in Holstein, where his father seems to have been a small farmer, and in a Mississippi river town, to which the family migrated, are most attractive, and put the reader in a good mood straight away. The second part is a technical exposition of his researches on coronary circulation and problems of cardiac action, which were conducted by himself assisted by a band of enthusiastic disciples, most of whom became renowned as professors in other universities or as directors of research. It is true that these contributions to our knowledge of circulatory dynamics can be read in the original papers; but Wiggers has done a real service in epitomizing them and revising them with the added knowledge given by further experimentation and thought. Moreover, the reading of the original articles would give no idea of the author as editor, teacher and organizer. Here we have a veritable treatise on the physics and physiology of the heart and blood vessels, given with refreshing clarity and free from the least suspicion of favouritism to any school or country. It would be impossible in a review to cover the ground here presented; the book must and will be read by those interested in the subject. One feature unique in medical literature is the series of short verbal sketches of the distinguished physiologists whom he met. If there is any bias in these, it is on the side of kindliness. Only one acidulous remark occurs: "G. V. Anrep . . . gave me the impression that he was the type of individual who could be suave when the recipient of courtesies, but diffident when he was expected to be the donor." Future historians of cardiology and physiology will be grateful for these vivid portraitures. A sense of humour pervades the whole book. One amusing incident is reported. Wiggers, in his investigations of heart sounds and especially in their recording, found that the French condom was thinner and more serviceable for experimentation than the American, so he obtained a liberal supply in Paris; but, alas, the Customs officer in the United States port of arrival impounded them as prohibited imports, and Wiggers had an anxious time explaining their intended use. The English is flexible and shows attention to literary form; the printing is excellent and the proof-reading good. On page 142 "*inhibition*" should be "imbibition", whilst some faulty Latin on page 381, attributed to Professor Solimann, can probably be placed on the broad shoulders of the compositor. But these are trifles, and do not mar a very great book.

The Year Book of the Ear, Nose and Throat (1958–1959 Year Book Series). Edited by John Lindsay, M.D.; with a Section on Maxillofacial Surgery edited by Dean M. Lierle, M.D., and William C. Huffman, M.D.; 1959. Chicago: The Year Book Publishers. Melbourne: W. Ramsay (Surgical), Limited. 7¼" × 5", pp. 400, with 113 illustrations. *Price: 82s. 6d.*

As in previous years, this Year Book is edited by John R. Lindsay, and has a section on maxillo-facial surgery edited by Dean M. Lierle and William C. Huffman. This year there is no introduction, and in the section on "The Ear", the sub-heading "Tubal Function and Inflammatory Ear Disease" has had added to it "Facial Paralysis and Tumors". There has been no change in the sub-headings in the section on "The Nose and Throat", whilst the section on "Maxillofacial Surgery" has been given a series of sub-headings of its own in the table of contents. This Year Book adequately covers twelve months' literature on the ear, nose and throat. The editor's comments, though not lengthy, are apt and interesting.

The Year Book of Drug Therapy (1958–1959 Year Book Series). Edited by Harry Beckman, M.D.; 1959. Chicago: The Year Book Publishers. Melbourne: W. Ramsay (Surgical), Limited. 7¼" × 5", pp. 276, with illustrations. Price: 82s. 6d.

WE have learnt to expect from the pen of Harry Beckman, editor of the "Year Book of Drug Therapy", some introductory remarks of a surprising (sometimes startling) nature. This year he has contented himself with presenting a "partial" list of the institutions from which emanated some of the original work presented in this book "in brief essence". He affirms that he does not keep a precise count "of the number of journals seen and articles read in making selections for the Year Book". He does not want to know what these numbers are, "for they might convict me of some sort of compulsive quirk". For those who are interested, in the present volume there are "493 articles from 23 countries and 108 journals"—a formidable total, but not surprising in view of the endless making of new drugs. Once more, hospital infections due to resistant staphylococci come in for comment, and several papers suggesting methods of control are summarized.

This is always a valuable "Year Book", since it gives recent information on newly-introduced drugs and on old friends for which new uses are being found. It is a book of reference that every clinician could have with advantage. The present volume is no exception.

The Rewards of Medicine and Other Essays. By Hugh Barber; 1959. London: H. K. Lewis & Co. Limited. 8¼" × 5", pp. 144. *Price: 15s. (English).*

THIS book is a collection of separate essays, four from The Practitioner and most of the others from Guy's Hospital Gazette. The author makes no claim to discovering a new syndrome, advancing a new pathological hypothesis or suggesting a new line of treatment; the aim and usefulness of the book lie elsewhere. We have here an elderly, wise, kindly and honest practitioner, who has a wide knowledge of English literature and history, and who writes in the tradition of Wendell Holmes. Longfellow,

in his poem "The Day is Done", voices the desire of many men, alive to the beauty of true poetry, not to choose, when weary with work or anxiety, a literary creation which is challenging or sonorously stimulating, just something to "quiet the restless pulse of care", and this is precisely what this volume offers. The reader will find evidence of historical research, particularly in the essays dealing with Smollett, Erasmus Darwin and the body snatchers, but the robe of learning is worn gracefully. In almost every page there is a bright story drawn from the author's experience or from literature, a story to remember and possibly to retail.

A Clinical Introduction to Heart Disease. By Crighton Bramwell, M.A., M.D., F.R.C.P.; 1959. London, New York and Toronto: Oxford University Press. 8¼" × 5¼", pp. 240, with 61 illustrations. Price: 39s. 3d.

WHAT a delightful experience it becomes to read a clinical handbook by a master cardiologist, after a tedious period of papers and books on hæmodynamics, electronic physics and statistics! Not that these matters are unimportant; but a small, easily read and practical account of the experiences and conclusions of a senior clinician is both welcome and valuable. Professor Crighton Bramwell's distinguished career as a cardiologist at Manchester has been a blend of carefully documented bedside experience and of highly important contributions to cardio-vascular physiology. His own research has bridged the interval between the relatively crude recordings of cardio-vascular events, which the famous pioneers such as Erlanger, Mackenzie and Lewis produced, and the complex modern electronically produced tracings of today.

This small book is designed specifically for students and for resident medical officers or general practitioners wishing to revise briefly their basic cardiology. The author explains in his preface that he has attempted to present the basic principles of cardiology to young doctors in their pre-registration year, who may wish to consider cardiology as their vocation—a commentary on the remarkable emphasis which is now placed on early specialization in Great Britain. Professor Bramwell admits that he has made no attempt to cover the whole field, but has tried to lay down fundamentals of diagnosis, treatment and prognosis, as he sees them after a very active life as a teacher, physiologist and consultant. For such a small volume, he has succeeded in introducing many historical references and many clinical illustrations from his own case notes, in which he frankly admits his own occasional error. The structure of the book is rather unusual; for instance, "The Normal Heart" constitutes the second-last chapter; the first is entitled "The Clinical Approach". However, one is not conscious of any mental discomforture by reason of the departure from a more traditional sequence. Throughout all chapters one feels the atmosphere of the author talking in his study rather than in the lecture room. Some time is passed in consideration of basal physical principles of the pulse, murmurs, blood pressure and the arrhythmias. The best sections are those which reveal the author's own philosophy in dealing with patients and relatives, and his insistence on the history, the progression of the disease and the bedside findings. He deprecates the use of loose diagnosis, especially "false angina", "the tired heart" and so forth, and yet sanctions the term "heartache". The chapter on blood pressure and the proper method of recording it is particularly valuable. In detail, there is hardly a statement with which one can disagree or which one can criticize. He rightly emphasizes that the quality of a murmur, well appreciated by the human ear, is as important as its timing. "Summation gallop" is accorded a serious significance in all cases; we think it can be benign in some normal hearts at high rates of contraction. Similarly, it has not been our experience that the diastolic murmur of mitral stenosis often disappears with the development of pulmonary hypertension, nor have we found auricular fibrillation or the Lutembacher syndrome common in atrial septal defects. Too little is said as to the selection of patients for mitral valve surgery, on the treatment of ventricular tachycardia and on the hypotensive management of essential hypertension. We agree on the value of venesection in the last-mentioned disorder, whether the effect is psychotherapeutic or not.

The parts of the book we most admire concern the attitude of the author towards the supreme importance of clinical aids to diagnosis and prognosis, his emphasis on optimism, the importance of rest in treatment, the assessment of the patient and his environment, and his emphasis on the variation of the normal. It almost makes one wish that all great cardiologists like Bramwell should be forced to set down their conclusions and their attitudes, as they have done here; for his rich store of experience, illuminated by his unusual gifts of observation, industry and lucid explanation, are now preserved for many generations of future physicians working in his chosen field.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Right-Left Discrimination and Finger Localization: Development and Pathology", by A. L. Benton, Ph.D.; 1959. New York: A Hoeber-Harper Book. 9¼" × 6", pp. 200, with illustrations. Price: $7.00.

The author is Professor of Psychology in the State University of Iowa.

"Hypertensive Disease: Diagnosis and Treatment", by S. W. Hoobler, M.D.; 1959. New York: A Hoeber-Harper Book. 9¼" × 6", pp. 363. Price: $7.50.

The author is director of the Hypertensive Unit, University of Michigan Hospital.

"Major Endocrine Disorders", by S. L. Simpson, with the collaboration of A. S. Mason and G. I. M. Swyer; Third Edition; 1959. Melbourne: Oxford Press. 8¼" × 5¼", pp. 467, with illustrations. Price: 72s.

A fully revised edition, still planned to serve the clinician.

"Strong and Elwyn's Human Neuroanatomy", by R. C. Truex; Fourth Edition; 1959. Baltimore: The Williams and Wilkins Company. 10" × 6¾", pp. 524, with 363 illustrations. Price: £5 10s.

The present author has aimed to maintain Professor Elwyn's original objective—to keep this volume a "student textbook".

"History of the Second World War: United Kingdom Medical Series", Editor-in-Chief, Sir Arthur S. MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S., "The Royal Air Force Medical Services", edited by Squadron Leader S. C. Rexford-Welch, M.A., M.R.C.S., L.R.C.P., R.A.F., Volume 3, "Campaigns"; 1958. London: Her Majesty's Stationery Office. 9¼" × 5¾", pp. 755, with many illustrations. Price: 15s.

The final volume on the R.A.F. Medical Services.

"Time Distortion in Hypnosis: An Experimental and Clinical Investigation", by L. F. Cooper, M.D., and M. H. Erickson, M.A., M.D.; Second Edition; 1959. Baltimore: The Williams and Wilkins Company. 9" × 6", pp. 217. Price: 44s.

A revised edition with some significant new material added.

"Involutional Melancholia: An Etiological, Clinical and Social Study of Endogenous Depression in Later Life, with Special Reference to Genetic Factors", by A. Stenstedt, M.D.; First Edition; 1959. Copenhagen: Einar Munksgaard. 9¼" × 6¼", pp. 71. Price not stated.

The title is self-explanatory.

"Conquering Physical Handicaps: Official Proceedings of the First Pan-Pacific Rehabilitation Conference held in Sydney, Australia, November 10-14, 1958", published by The Australian Advisory Council for the Physically Handicapped, A Member of The International Society for the Welfare of Cripples; 1959. 8¼" × 5", pp. 617, with many illustrations. Price not stated.

A somewhat condensed report of the conference.

"The Degenerative Back and its Differential Diagnosis", by P. R. M. J. Hanraets, M.D.; 1959. Amsterdam, London, New York, Princeton: Elsevier Publishing Company. 8¼" × 6", pp. 700, with many illustrations. Price: £5 5s.

Translated from the Dutch. The author is a neurosurgeon.

"The Plasma Proteins: Clinical Significance", by P. G. Weil, B.A., M.D., C.M., M.Sc., Ph.D.; 1959. Philadelphia, Montreal: J. B. Lippincott Company. 7¼" × 4½", pp. 149. Price: £1 18s. 6d.

A general review.

The Medical Journal of Australia

SATURDAY, OCTOBER 24, 1959.

RUBELLA IN PREGNANCY.

THE recent correspondence[1] on rubella in pregnancy in the *British Medical Journal* revealed that it is a subject on which there is still a considerable amount of confusion and uncertainly. Some of the statements in the article[2] which provoked this correspondence were certainly surprising in view of the fact that recent surveys have all tended to show that the risks of fœtal damage resulting from rubella in pregnancy are substantially less than had been originally suggested by the work of Gregg and Swan. One of the most recent of such surveys to go into print is one by V. P. Coffey and W. J. E. Jessop[3] of Dublin. This is a small prospective survey based on an epidemic of rubella which occurred in Dublin in the first half of 1956, and concerns 26 mothers who contracted rubella during their pregnancy, and 49 who were rubella contacts during pregnancy: the latter were included because of the frequency of subclinical infections. The numbers are too small to form the basis of any major conclusions, but the results fit in well with those of other recent prospective surveys. Of 10 mothers who contracted rubella during the first trimester, one had a miscarriage (the only one in the entire series), one had a baby with a talipes deformity, and the baby of another had a congenital cataract. Out of 14 pregnancies in women who had rubella later in pregnancy, one ended in the birth of an anencephalic fœtus and in another case the baby had a talipes deformity. It seems highly improbable that rubella occurring after the first trimester could be held responsible for an anencephalic fœtus, and talipes is not generally recognized as among the deformities which may result from infection early in pregnancy; but the real interest of these figures lies in the fact that even among those women who developed rubella in the first trimester, seven out of ten had perfectly normal babies. In spite of the number of prospective surveys of which the results have now been published, it is still not possible to make any accurate statement as to the chances of congenital malformations occurring after maternal rubella early in pregnancy. This is because of the difficulty in obtaining a sufficiently large number of cases by prospective survey to provide a basis for firm statistical conclusions, and many of the published surveys are in various ways incomplete. Congenital deafness is by far the commonest defect resulting from maternal rubella, yet A. D. M. Jackson and L. Fisch[1] have published the only series in which the children concerned have been followed for four years and have had their hearing properly investigated at the end of that period. In this series 14 out of 46 children, whose mothers had rubella during the first 16 weeks of pregnancy, suffered from congenital deafness, the deafness being unilateral in five of these. Coffey and Jessop state that recent prospective surveys of the results of pregnancies in which rubella has been diagnosed in the first trimester show an incidence of serious defect varying from 10% to 30%, but for reasons already stated, even this approximation has little meaning. Perhaps the clearest indication of the risks is given by Bradford Hill and his colleagues[2] in a table in which they correlate the results of their own and of the three other surveys from which adequate data were available; from this it is seen that serious defects occurred in six out of 12 infants whose mothers developed rubella in the first four weeks of pregnancy, in five out of 20 infants whose mothers developed rubella in the second four weeks, and in three out of 18 infants whose mothers developed rubella in the third four weeks. However, in none of these series was the occurrence of congenital deafness fully investigated, and it may be presumed that some of these children who were otherwise normal would have had some impairment of hearing; only those with severe degrees of congenital deafness are likely to have been picked up by clinical observation alone at such an early age. It appears that the risk of serious deformity affecting the heart, brain or eyes is considerably greater if the disease is contracted in the very early weeks of pregnancy. On the other hand, the incidence of congenital deafness is apparently greatest among those whose mothers had rubella between the ninth and fourteenth weeks of pregnancy (Jackson and Fisch).

It is therefore to be hoped that the painstaking efforts of those who have been collecting data for prospective surveys will presently result in the emergence of some more accurate information. As is widely known, the Department of Obstetrics and Gynæcology at the University of Melbourne have had such a survey in progress for some time (this survey is described in an article by D. B. Pitt in the Journal of February 23, 1957), and it is hoped that their efforts were well supported by those doctors who encountered cases of rubella in pregnancy in their practices during the recent Australia-wide epidemic, which is still smouldering in Victoria, and possibly in New South Wales (though, owing to the policy of the Health Department of that State, statistics are not in that case available). To maintain a proper perspective, it is perhaps appropriate to conclude by restating Pitt's remarks to the effect that maternal rubella is in fact a rare cause of congenital defect, and accounts for only a

[1] *Brit. med. J.*, 1959, 1: 921 (April 4), *et sequitur*.
[2] *Brit. med. J.*, 1959, 1: 686 (March 14).
[3] *Irish J. med. Sci.*, 1959, No. 397: 1 (January).

[1] *Lancet*, 1958, 2: 1241 (December 13).
[2] *Brit. J. prev. soc. Med.*, 1958, 12: 1 (January).

very small proportion of all such defects seen, of whatever kind. Pitt records that of 180 consecutive cases of congenital malformation recorded at the Royal Women's Hospital, Melbourne, during the year 1955-1956, not one was associated with a history of maternal rubella.

Current Comment.

SOME ASPECTS OF RADIATION BIOLOGY AND CANCER RESEARCH.

THE papers presented at the twelfth Annual Symposium on Fundamental Cancer Research, held at Houston, Texas, in 1958, have been published under the rather misleading title "Radiation Biology and Cancer".[1] Such an all-embracing title suggests a text giving complete subject cover. However, the volume comprises a collection of 33 papers of rather diverse interest within the fields of radiobiology and experimental cancer research. Some are of extraordinary topical interest.

Jacob Furth writes an instructive paper on radiation neoplasia and endocrine systems. He states that radiation will produce leukæmia and other tumours in animals much more readily than in man. The theory of somatic mutation as a cause of these cancers is not acceptable. Tumours in a previously balanced endocrine system arise, firstly, from some deficiency in a restraining force; for example, destruction of the thyroid in rats causes pituitary tumours. Here the withdrawal of thyroxin causes the pituitary to be stimulated and later to develop tumour. Secondly, excessive stimulation by a peripheral hormone may cause a pituitary tumour. Excess œstrin can produce a mammotrophic tumour. The acidophil pituitary cells which appear in the mammotrophic tumour have granules of two sizes, the smaller probably the growth-stimulating hormone, the larger probably the mammotrophic hormone. The direct pituitary hormone stimulating the breast is the mammotrope, produced by œstrin acting on the pituitary. Thirdly, altered response to normal hormones by hormone-responsive cells may result in production of neoplasms. Radiation to certain tissues may be a cause of such altered response; carcinomas occur more readily in breasts of certain irradiated animals than in controls, adrenotropic tumours occur in irradiated pituitary glands, and rarely adrenal tumours may appear in treated suprarenal glands. In all cases the normal hormones appear to cause stimulation in the abnormal cells, which ultimately results in tumour formation.

In a discussion of the effects of radiation on neoplastic cells and their radiosensitivity, T. C. Evans suggests that the phenomenon of increased radioresistance of irradiated but unkilled cells of a tumour, which ultimately grow to form a recurrence, may be due to a change in the surviving cells from diploid to tetraploid chromosome numbers. There is reason for the belief that cells containing increased chromosome numbers may be more radioresistant. Rubin quotes the work of Gaulden, who used a microbeam of ultraviolet light to irradiate selected portions of single cells. The most radiosensitive structure in the cell was found to be the nucleolus; and of the chemical systems, that which synthesized ribonucleic acid was the most radiosensitive.

L. O. Jacobson considers hæmatopoietic effects of irradiation. In 1949 it was shown that spleen shielding or subsequent injection of spleen or embryonic marrow suspension enhanced the survival of mice exposed to otherwise lethal doses of radiation. Marrow recovery was complete in the injected animals by the tenth day; the graft cells recolonized the irradiated marrow. A marrow suspension was the most efficacious agent for ensuring survival. Embryonic or baby marrow suspensions were more effective than adult suspensions, as the former had not the complicated antigenic capacities of the latter. Later it was demonstrated that the irradiated mouse could be saved temporarily by heterologous marrow suspensions (adult guinea-pig to mouse). However, late death always followed. But this late death could be prevented by the use of heterologous embryonic marrow suspensions. The irradiated animal has its immune mechanisms destroyed, adult marrow grafts save the animal, but antigenic reactions of this donor tissue ultimately kill the animal. The use of embryonic heterologous marrow, which is free from such antigenic activity, enables the irradiated animal to survive. From these experiences the theory of "acquired tolerance" of embryonic tissues to adult tissue antigens has been developed.

In an approach to the problems of marrow replacement therapy after irradiation of patients with leukæmia, H. H. Trenton states that an irradiated mouse subsequently protected with an injection of rat marrow may survive with its red cells, white cells, platelets and lymphocytes and even its serum gamma globulins of rat donor origin. In this state it will accept a rat skin graft, but not a mouse skin graft. If human leukæmia is treated along these lines, grave problems arise. Firstly, the leukæmic tissue may be more radioresistant than other normal tissues, and the patient may die of acute bowel necrosis while the disease persists. Secondly, marrow replacement in the human would be of homologous type. Irradiated mice protected by homologous marrow injections suffer late death in a high proportion of cases. This may be due to two causes. If only a sublethal dose of whole body irradiation has been given and a subsequent homologous marrow protective injection is administered, some portions of the animal's original marrow may be found to survive, which after recovery causes antigenic reactions with the death of the animal. This is the syndrome of "grafted marrow rejection". Therefore in treatment of human leukæmia, sublethal whole body irradiation would carry great danger from this cause. If a full lethal whole body irradiation dose was administered, death still might occur, because the donor marrow antigens would act against the recipient to cause a late death. The only known way of overcoming such "homologous marrow graft disease" is to use a suspension of embryo or baby marrow, which would allow immunological tolerance to be acquired by graft as well as by the host. Metcalf has found that the thymic medulla elaborates a factor which stimulates lymphocyte production. It is present in relatively high concentration in mice strains with high spontaneous incidence of leukæmia and is not detectable in the blood of low incidence leukæmic strains.

W. C. Moloney considers the known cases of the induction of leukæmia in man by radiation. In the 20-year period from 1929-1949 5% of American radiologists died of leukæmia compared with a 0·5% incidence amongst other medical practitioners. (No such incidence of leukæmia has been found amongst British radiologists.) Leukæmia has occurred in association with spondylitis ankylopoietica following irradiation, although the incidence is, in fact, very low. Seven patients with thyroid disease treated therapeutically with I^{131} are also known to have developed leukæmia; four of these were suffering from carcinoma of the thyroid, three from hyperthyroidism, the latter receiving very low dosages. Simpson is quoted for blaming irradiation of the thymus in babies for an increased incidence of leukæmia. Stewart is reported as stating that leukæmia is twice as common among the children of mothers who have had radiological pelvimetry as among children of mothers not so examined. In the recorded cases the whole body fœtal dose varied between 2 r and 10 r. The cases of leukæmia which followed whole body atomic bomb radiation are well known. Radiation leukæmia may appear as the acute myeloid form, rarely as the subacute form, and frequently as the chronic myeloid variety. Chronic lymphatic leukæmia never occurs. The latent period may be from one to nine years after the exposure. Occasionally the

[1] "Radiation Biology and Cancer", editor unnamed, University of Texas Press, Austin, 1958, pp. 493 including index.

onset may be with leucopenia or with pancytopenia, which may mimic aplastic anæmia or myelofibrosis. The mechanism of production may be an induced deficiency state of a marrow cell regulating factor occurring in individuals with differing degrees of susceptibility.

W. J. Burdette discusses the factor of susceptibility in relation to cancer development by an individual. He points out that, as yet, there is no conclusive evidence that somatic mutations are the basic causes of cancer. A somatic mutation could result from a change in gene position on a chromosome or from an actual alteration in the gene itself. In general, known carcinogenic agents fail to produce mutations in *Drosophila*, while substances which will readily cause mutations in these flies are not carcinogenic. Genetic factors are responsible for individual susceptibility, and susceptibility genes exist. These genes are found widely distributed among the chromosomes. Mutation studies in *Drosophila* indicate that the gene changes are complex and are not explicable in terms of a simple deletion or addition of chromosome material.

W. J. Schull states that human radiation exposure results from terrestrial background radiation, from medical uses of radiation, from fallout from weapons testing, from occupational exposure or from atomic power plants and their radioactive waste disposal. He examines every known way in which increase in radiation exposure could cause detectable changes in the present world population. Among the variables which have been studied are the frequency of male births and of major congenital malformations, and perinatal and infant mortality; birth weight variations and selected anthropometric measurements have been examined. Offspring of various exposed population groups have been investigated in detail. It is concluded that the only parameter of any present value as a measure of increased mutagenic rate resulting from greater parental radiation exposure is an alteration of sex ratio of the offspring. In the event of paternal exposure the sex ratio (males to females) would be augmented, since sex-linked lethal mutations would be distributed only to female offspring. In the event of maternal exposure, induced sex-linked dominant lethal mutations would cause equal reduction in frequency of both male and female births. Sex-linked recessive lethals would lead to a greater reduction in male births than in female births with a subsequent reduction in the sex ratio. The effect on male and female parents therefore is in opposite directions. If both parents are subject to radiation, there may be no effect on the sex ratio, though an over-all reduction in male births would probably occur because of the more frequent occurrences of sex-linked recessive lethals in the female parent.

D. E. Bergsagel and P. Grannopoulos have studied the anæmias associated with chronic lymphatic leukæmia and Hodgkin's disease. Increased hæmolysis is an important factor in the late anæmia associated with each of these diseases, while red cell life is often greatly shortened. By using isotopic methods which they fully explain, the authors have found that the rate of destruction by hæmolysis in these diseases is two to four times normal, but they state that a normal marrow should be able to cope with a rate of destruction six to eight times normal. The anæmia can be further accounted for by postulating reduced erythropoiesis. Another factor is a disturbance of iron metabolism with a relative serum iron deficiency. Here defects in mobilization of stored iron prevent production of sufficient hæmoglobin to compensate for the higher hæmolysis rate. In chronic lymphatic leukæmia deficient hæmatopoiesis is the major factor in the appearance of the anæmia. The red cells are produced more slowly, but adequate serum iron levels allow rapid hæmoglobin synthesis. The hæmolysis rate is increased, but this may be retarded by administration of prednisone, which also stimulates hæmatopoiesis. In Hodgkin's disease, increased hæmatopoiesis is found, but the serum iron levels are low from defective mobilization of stored iron, and so the erythrocytes are hypochromic. The shortened red cell life and the increased hæmolysis rate are other factors concerned in the late anæmia.

G. H. Fletcher reviews 1500 patients treated with megavoltage radiations for carcinoma of the cervix, of the mouth and of the bladder. His conclusions in regard to treatment of bladder neoplasms are closely in accord with recent English and Australian experience. High radiation dosage given to patients with extensive disease only increases the incidence of complications. Palliative techniques should be low in dosage prescription. He finds a definite increase in the incidence of contracted bladder after recent partial cystectomy when followed by heavy post-operative irradiation. The presence of bladder-neck obstruction or severe cystitis decreases local tolerance to radiation. Elderly women tolerate bladder irradiation poorly. Bladder surgery following heavy irradiation is associated with a high incidence of delayed healing. Radiation does not prevent recurrence in the superficial low-grade group of tumours subject to multicentric new tumour formation. These tumours should be treated by transurethral surgery as long as possible. Radical megavoltage radiation therapy has been of greatest benefit in the inoperable group of undifferentiated and squamous carcinomas.

THE EFFECT OF INGESTION OF ARACHIDONIC ACID ON SERUM CHOLESTEROL.

A great deal has been written on the effect of ingestion of saturated and unsaturated fatty acids on the cholesterol content of the blood plasma and this in turn on the incidence of atherosclerosis. It is widely believed that ingestion of the saturated fatty acids causes a rise in plasma cholesterol content and that ingestion of polyene fatty acids causes a fall, while oleic acid has no effect. The evidence for these views is strong, but some points are not yet clear. Linoleic acid with two double bonds and arachidonic acid with four double bonds have long been considered to be essential fatty acids in the sense that when not enough is ingested, serious symptoms appear. Arachidonic acid is considered to be the essential acid, linoleic acid being in part converted to arachidonic acid in the liver. Part of the linoleic acid ingested is burnt up in the ordinary way to give energy, and much of it goes to the making of lipoproteins. The functions of arachidonic acid in the body are not well known, but if the essentiality of the polyene fatty acid has any important connexion with the plasma level of cholesterol, one would expect that ingestion of arachidonic acid would cause a fall in the plasma level of cholesterol. To study this point A. Keys, J. T. Anderson and F. Grande[1] fed six middle-aged men with a concentrate of arachidonic acid for a period, and three controls comparable in body weight were given oleic acid; the plasma cholesterol level was observed during and for some time after the giving of the supplement. Sixteen capsules each of 0·5 gramme of the arachidonic acid concentrate were given daily, so that the subjects ingested four to five grammes of arachidonic acid daily. The work was carried out very carefully. After a trivial initial decline from previous control values, the serum cholesterol level rose during the last days of the administration of arachidonic acid, rose still further after cessation of the administration and continued to stay high for about two weeks. The number of subjects examined was small (this was conditioned by the availability of the arachidonic acid), but it is clear that the evidence offers no support for the idea that supplementing an ordinary diet with arachidonic acid will produce any important depression of the serum cholesterol level. Keys, Anderson and Grande present their views as to the possible cause of the rise in serum cholesterol level, but these are not supported by experimental evidence. Obviously the story of the parts played by polyene fatty acids in controlling the serum cholesterol level cannot yet be told in full, and it is not clear that the essentiality of the polyene fatty acids has anything to do with cholesterol level or with the incidence of atherosclerosis.

[1] *Amer. J. clin. Nutr.*, 1959, 7: 444 (July-August).

Abstracts from Medical Literature.

HYGIENE.

The Biological Effects of Vanadium.

C. Lewis (*A.M.A. Arch. Industr. Hlth*, May, 1959) studied the effect of 0·1 to 0·3 mg. per cubic metre of vanadium in breathed air on 24 workers and compared his results with previously reported studies. A detailed history and physical examination, analysis of urine, hæmatocrit estimation, electrocardiogram, estimation of vanadium content of urine, and serum cholesterol determination were made on these men and on a larger group of control subjects. The vanadium workers were found to have a significantly higher incidence of signs and symptoms referable to the irritative properties of vanadium dust. Irritation of eyes, nose, throat and respiratory tract was seen in 62% of vanadium workers. A green coloration of the tongue was observed in 37% of the exposed group. No evidence was found of chronic intoxication or injury attributable to vanadium exposure. The serum cholesterol levels of men exposed to and absorbing vanadium were significantly lower than those of the controls.

Agricultural Industry.

C. Berry (*Amer. J. publ. Hlth*, May, 1959) draws attention to the need for an occupational health service for people engaged in the agricultural industry. Some of the industrial hazards involved include increased risk of infection with animal diseases transmissible to man, modern high-powered complicated machinery, the use of veterinary pharmaceuticals and toxic chemicals, and varying physical factors in the external environment which can be satisfactorily controlled. Medical assistance and facilities and advice regarding avoidance of hazards are often not readily available. The author makes the following suggestions: (i) The hazards involved should be further investigated. Existing occupational health programmes should be expanded to serve agriculture better. (ii) Educational programmes at youth and adult levels should be devised for instruction and demonstration of safe and healthful work patterns. (iii) Doctors need to be orientated to the unique hazards of farming and alerted to their professional potentials in providing improved prevention, diagnosis, and treatment. (iv) There is a need for coordination of all medical services: physicians, hospitals, voluntary agencies, public health agencies, health and safety committees of rural organizations, schools, agricultural extension services, and any community services that may exist. (v) Manufacturers, builders, suppliers, fabricators, blenders, packagers and others should be encouraged to cooperate among themselves in taking measures to reduce potential hazards in the consumption of goods and services on the farm.

Health Problems of Epoxy Resins.

L. Bourne, F. Milner and K. Alberman (*Brit. J. industr. Med.*, April, 1959) have investigated health hazards associated with the use of epoxy resins. The chemistry of the epoxy resins and "curing" agents used with them is given. "Curing" agents include primary, secondary and tertiary amines, organic acids, acid anhydrides and the polyamide resins. All are irritants to a varying degree, except the polyamide resins. The authors suggest that injurious effects are due to the formation of substances with the properties of antibodies from the union of proteins and reactive parts of molecules of resins and curing agents. According to the authors, if this explanation is correct it has the following important practical consequences: (*a*) no resin and hardener system capable of reacting at normal temperatures can be regarded as physiologically inert; (*b*) it is impossible to produce a system which is completely non-toxic, since chemical and biological activity are inseparable; (*c*) minimum toxicity should be associated with minimum volatility of the components and with minimum solubility in skin secretions; (*d*) it seems to be an experimental fact that the risk of sensitizing an individual to these materials is proportional to the integrated exposure (concentration × length of exposure) to which he is subjected. Once an individual is sensitized, the slightest contact with the offending material will provoke an immediate reaction. The authors state that the risk of sensitization can therefore be minimized: (i) if pollution of the atmosphere is avoided; (ii) if the material is prevented from coming into contact with the skin; (iii) if, where contamination of the skin is unavoidable, suitable barrier cream is used to minimize the risks of penetration; (iv) if deposits of resin are not allowed to accumulate upon the skin but are cleaned off as frequently as circumstances permit. Details of the practical application of the above principles in industry are then given.

An Epidemiological Study of Congenital Malformations.

J. T. Gentry, E. Parkhurst and G. Bulin (*Amer. J. publ. Hlth*, April, 1959) have tabulated all recorded congenital malformations in children born during 1948 to 1955 in New York State, exclusive of New York City, the information having been obtained from birth and death certificates. The incidence of malformation was 13·2 per 1000 live births. Malformation incidence rates in some areas of the State were 20·0 or more. An independent compilation was made of all available geological data relating to deposits of material with high levels of radioactivity. Areas where extensive quantities of natural materials with relatively high levels of radioactivity were probably present had a malformation incidence rate of 15·8 per 1000 live births. The rate for other areas was 12·9. The neonatal mortality rate from malformations was found to be inversely related to the socio-economic status of fathers. However, there was no relationship between socio-economic status and the presence of radioactive materials. In areas where radioactive materials probably existed, the malformation rate was highest (16·9) in communities deriving their water supply from wells and springs and lowest (12·4) in those utilizing surface waters. In other areas the corresponding rates were 12·9 and 11·9. Field measurements of external environmental radiation levels were found to lie mainly in the range 8 to 12 μr per hour. Near exposed minerals they were as high as 40 μr per hour. Water from some springs and wells near igneous rock outcrops contained more radium 266 than usual. The authors suggest that the association of increased malformation rates with residence in areas containing materials with relatively high levels of radioactivity strongly suggests ionizing radiation as a primary ætiological cause of the malformations.

The Epidemiology of "Q" Fever.

L. Luoto (*Amer. J. publ. Hlth*, March, 1959) has summarized available information on the epidemiology of "Q" fever. He suggests that the incidence of this disease in human beings will increase because of increased incidence among animals, and of closer contact of human beings with animals, unless preventive action is taken. Human infection has resulted from occupational exposure to infected cattle, sheep and goats, from residence near infected premises and from infected milk. Commercially pasteurized milk has been shown to contain viable *Coxiella burneti*. Because of difficulty in confirming the diagnosis, many cases of "Q" fever are not diagnosed. The author considers that mass immunization may be effective, but is not practicable as a preventive measure, and that therefore prevention of "Q" fever depends on its control in animals. Infection in animals is mainly from inhalation of air-borne "Q" fever rickettsiæ, which are usually derived from infected material discharged at parturition. They are very resistant, and render the area infective for long periods. In some areas 75% of herds and 45% of cattle investigated gave positive serological results for "Q" fever. To determine whether the incidence of "Q" fever is increasing in an area, the author considers that surveys of human beings and animals for evidence of "Q" fever infection should be done and if then indicated, control measures adopted. He also considers that the capillary tube agglutination test is highly specific and sensitive for *C. burneti* antibody and could be easily used to determine the extent of "Q" fever infection in an area.

Medical Examinations for Public Safety.

P. A. B. Raffle (*Brit. J. industr. Med.*, April, 1959) discusses the value of pre-employment medical examination standards in maintaining public safety, and he refers to clinical conditions that may render a man dangerous to the public safety. The discussion is based on experience of the London Transport Medical Service where the aim of the pre-employment medical examination of drivers is to ensure that drivers have adequate eyesight, are physically capable of handling controls, and are not suffering from conditions liable to cause sudden loss of consciousness or excessive fatigue at the end of a day. From 1950 to 1957, 18,003 applicants were examined and 18·6% were rejected, 5·3% on general medical grounds. Substandard vision or defective colour vision was the cause of 71% of the rejections and cardio-vascular disease of 1·4% of rejections. Subsequent routine medical examinations of employed

drivers indicated that 9·2% of those examined were medically unfit. The two most frequent causes for unfitness were disease of the circulatory system and functional nervous disorder. In conclusion, the author stresses the importance of cardio-vascular lesions in rendering a person unfit for a position involving public safety, and states that in detecting these a careful assessment of the patient's fitness to resume his occupation after a spell of sickness is equally as important as routine periodic medical examinations.

Pulmonary Fibrosis in an Aluminium Worker.

J. MITCHELL (*Brit. J. industr. Med.*, April, 1959) reports the case of a patient with non-nodular pulmonary fibrosis which he considers was due to a susceptible subject inhaling high concentrations of fine aluminium dust. The patient, after leaving school, worked as an agricultural labourer until 19 years old. He then worked for two years with two other men on an eight-hour shift rota, attending stamping machines that produced finely divided aluminium powder. The air near the machines contained approximately 10 mg. of dust particles below 5μ in size per cubic metre. In addition to aluminium, the dust contained stearine in quantities up to 0·5% of the total weight. The patient developed a cough and breathlessness which disabled him. He grew progressively worse and died nine months after ceasing to work. At post-mortem examination, the lungs showed generalized non-nodular fibrosis and emphysema, and contained 640 p.p.m. of aluminium, estimated as Al_2O_3. The heart was enlarged; other organs were normal and there was no evidence of other disease.

PHYSICAL MEDICINE AND REHABILITATION.

Contractures in Muscular Dystrophy.

K. C. ARCHIBALD AND P. J. VIGNOS (*Arch. phys. Med.*, April, 1959) have reviewed the status of 43 patients with muscular dystrophy seen during the past three years in the muscular dystrophy clinic of the University Hospitals of Cleveland. The authors state that a well outlined, conscientiously applied exercise and stretching programme effectively retards the natural progression of joint contractures in muscular dystrophy when it is started early in the course of the disease. Environmental factors are directly related to the success of a home programme. Ilio-tibial band contractures appear to have an important influence on joint contractures and deformities, although little attention has been focused on their role in this disease. Bracing in the treatment of patients with progressive muscular dystrophy has been shown to retard deterioration to a wheel-chair status. It also appears to be helpful in retarding the development of contractures. The occasional judicious use of surgery may be justified as a possible adjunct. The present management of muscular dystrophy is frequently discouraging, frustrating and unsatisfactory. Nevertheless, every attempt should be made to retard the natural course of the disease by the early initiation of an appropriate programme. The authors emphasize the need for a continued energetic analysis of methods to control the progression of this baffling disease.

Work Classification in Heart Disease.

S. S. SOBIN *et alii* (*Arch. phys. Med.*, April, 1959) present an appraisal of the work of the Los Angeles County Heart Association work classification unit, which has been in operation for almost four years. In that period it has successfully shown to employers, personal and industrial physicians and others that many patients with cardio-vascular disease are capable of working. Several significant insights have resulted from this experience. The first is that a demonstration of ability to work is not the same as a demonstration that heart patients can be rehabilitated. In fact, the demonstration of work ability becomes the justification for rehabilitation services. The second is that demonstration does not mean simply showing that many heart patients can work; it must also mean changing community attitudes and patterns of service. This necessitates such activities as publicity, training, observation and extension of services. This concept also has implications for the length of time required for a successful demonstration. The authors state that the unit clearly has a continuing function, which will require a number of years to achieve—to change the popular misconception that heart patients are unable to work.

Bladder Management in Traumatic Paraplegia.

P. A. MORALES AND R. S. HOTCHKISS (*Arch. phys. Med.*, April, 1959) state that the need for assiduous bladder care from the very beginning of paraplegia is of the utmost importance, and its unremitting continuance throughout the paraplegic's life should be emphasized. Many complications may thus be averted and rehabilitation of the patient greatly accelerated. The authors discuss treatment under the following headings: (i) initial treatment; (ii) bladder training; (iii) high residual urine; (iv) urinary infection; (v) calculus formation; (vi) vesico-ureteral reflux and hydronephrosis; (vii) hypotonic and hypertonic bladder; (viii) follow-up care. They state in conclusion that dangerous renal lesions may develop insidiously, and a bladder that empties well is no guarantee of the permanency of good renal function.

Painful Arm and Shoulder.

P. A. NELSON (*J. Amer. med. Ass.*, February 21, 1959) discusses the physical treatment of painful arm and shoulder. Diagnosis of the cause is important. Painful arm and shoulder may not be associated with local disease, and in such cases there is no limitation of movement of the shoulder joint. Cervical spondylitis and compression of the brachial plexus or subclavian artery or vein by a cervical rib or the scalenus muscle are well-known causes. Neck-lash injury, muscle strain and fibrositis, and visceral disease are also to be considered. Physical treatment in these conditions is to be directed towards the cause. In osteoarthritis of the spine with cervical radiculopathy, physical treatment by the local application of heat and sedative massage to the neck and shoulder are helpful. Posture training, neck exercises and cervical traction by the Sayre head halter with the patient in a sitting position, applied two or three times a week for a month, should follow. Cervical traction is considered most important, and is applied for three, five or 10 minutes at tensions of 25 to 80 lb. in the physiotherapy department. The patient should be given a head halter to use at home at tensions of 20 to 30 lb. In the cervico-thoracic outlet syndrome operation is contraindicated without first giving an intensive programme of physical therapy for one to three months. This consists of the local application of heat and massage, posture training emphasizing the position of the shoulders, and posture exercises to strengthen the erector spinæ and rhomboid muscles. Patients should avoid sleeping with their hands above their heads and avoid activities which aggravate their symptoms. Neck-lash injury, often caused by injury from rear-end car collisions, causes pain radiating from the neck into the shoulder and arm. Heat, massage, posture training, exercises of the neck and cervical traction may be needed, but too much treatment should be avoided in view of the psychological effect which occurs in association with litigation. Muscular spasm may occur in association with kyphosis, sloping shoulders and forward position of the head, with resultant aching in neck and shoulders and upper part of the back. The ache in this case becomes worse as the day goes on. Pain with limitation of movement of the shoulder is found with periarthritis, calcified tendinitis, bursitis, rupture of the rotator cuff, the bicipital syndrome, the shoulder-hand syndrome, rheumatoid arthritis, contractures due to immobilization, acute trauma and neoplasm. Physical therapy in these cases is directed to the shoulder and arm. Heat, massage, passive or active movement and gentle stretching are advised. The author does not think that the form of heat applied in treatment is very material; a hot-water bag is often just as helpful as one of the many forms of electrical heat. Ultrasonic diathermy is the most recent method of applying heat electrically, and is used for five to 10 minutes with a current of up to 1·5 watts per square centimetre, utilizing the so-called stroking technique.

Neurotripsy for Respiratory Embarrassment after Poliomyelitis.

H. E. BILLIG, JR. (*Arch. phys. Med.*, June, 1959) states that in poliomyelitis, residual respiratory embarrassment may be the result of loss of sufficient motor nerve axons of the phrenic nerves to reduce the innervated diaphragmatic muscle fibres to below the point of providing enough power to aerate the lung properly. The denervated muscle fibres (about 125 per motor nerve axon) do not necessarily degenerate, but atrophy, and are capable of restoration to function if they are reinnervated by increased arborization of the residual intact motor nerve axons. To do this, the author crushes the phrenic nerve above the clavicle, a procedure which he terms "neurotripsy". Two typical cases in which this method was used are presented.

British Medical Association.

SOUTH AUSTRALIAN BRANCH: ANNUAL MEETING.

THE annual meeting of the South Australian Branch of the British Medical Association was held on June 24, 1959, in the Verco Lecture Theatre, Institute of Medical and Veterinary Science, Frome Road, Adelaide, DR. C. C. JUNGFER, the President, in the chair.

ANNUAL REPORT OF THE COUNCIL.

The annual report of the Council was received and adopted. The report is as follows.

The Council presents the following report of its activities during the past year.

At the annual general meeting of the Branch, held on June 25, 1958, the following officers and members were elected for the ensuing year:

President: Dr. C. C. Jungfer.

Vice-President: Dr. G. T. Gibson.

Honorary Treasurer: Dr. J. M. Dwyer.

Honorary Medical Secretary: Dr. Ronald Hunter.

Ordinary Members of Council: Group A—Dr. N. J. Bonnin, Dr. N. Halloran and Dr. R. C. Heddle. Group B—Dr. John Jeffries (Millicent).

At the first Council meeting of the new year, held on July 3, 1958, the following subcommittees were appointed:

Scientific: Dr. Noel Bonnin and Dr. R. G. C. de Crespigny.

National Health Service: Dr. L. R. Mallen, Dr. C. O. F. Rieger, Dr. R. N. C. Bickford and Dr. R. C. Heddle.

Ethics: Dr. C. O. F. Rieger, Dr. J. M. Dwyer, Dr. C. C. Jungfer, Dr. R. M. Glynn, Dr. P. W. Verco and Dr. R. C. Heddle.

Parliamentary Bills: Dr. L. R. Mallen and Dr. C. O. F. Rieger.

Library: Dr. P. W. Verco, Dr. R. Hunter, Dr. R. G. C. de Crespigny and the Honorary Treasurer (ex-officio).

Salaries: Dr. L. R. Mallen, Dr. R. M. Glynn and Dr. C. O. F. Rieger.

Medico-Pharmaceutical Liaison Committee: Dr. R. Hunter, Dr. C. O. F. Rieger and Dr. N. Halloran.

Tuberculosis Standing Committee: Dr. R. C. Angove, Dr. J. L. Hayward, Dr. K. S. Hetzel, Dr. H. D. Sutherland, Dr. J. G. Sleeman and Dr. P. S. Woodruff.

Standing Committee on Public Health: Dr. I. B. Jose, Dr. C. C. Jungfer, Dr. J. E. McCartney, Dr. G. Viner Smith, Dr. J. L. Stokes, together with a representative from the Department of Public Health, with power to coopt.

Standing Committee on Hospitals: Dr. I. B. Jose, Dr. R. H. Elix, Dr. R. G. C. de Crespigny, Dr. J. R. Magarey, Dr. L. R. Mallen, and the president-elect, with power to coopt.

The President, Immediate Past President, Vice-President, Honorary Treasurer and Honorary Medical Secretary are ex-officio members of all committees other than the Ethics and Standing Committees. The President and Honorary Medical Secretary are ex-officio members of the Ethics and of all Standing Committees.

Attendances at Council and Committee Meetings.

Dr. J. M. McPhie attended five meetings in his capacity as local representative of the Editor of THE MEDICAL JOURNAL OF AUSTRALIA. During his temporary absence abroad, Dr. C. G. Wilson attended four meetings in his stead.

Five meetings of the Building Committee, under the Chairmanship of Sir Henry Newland, have been held during the year.

Three meetings of a special subcommittee of the Council and representatives from the honorary staffs of teaching hospitals and the Faculty of Medicine were held during the year to consider the policy of the medical profession regarding the administration of teaching hospitals in South Australia.

Monthly Scientific Meetings.

Scientific meetings have been held during the year as follows:

1958.—July 31: "Medical Secrecy"; speaker, Dr. D. P. O'Connell; discussion opened by Dr. C. O. F. Rieger. August 28: "Failure to Thrive in Infancy"; speaker, Dr. Howard Williams; discussion opened by Dr. R. N. C. Bickford. September 25: "Anæsthetic Emergencies"; speaker, Dr. J. A. Ferris. "Fluid and Electrolyte Balance"; speaker, Mr. J. A. O'Brien; "Indications for Surgery of the Abdominal Aorta and Large Vessels", speaker, Mr. D'Arcy Sutherland. October 30: Clinical meeting, Repatriation General Hospital. November 27: "The Management of Surgical Extra-Pulmonary Tuberculosis", presented by Mr. O. W. Leitch and Dr. R. Munro Ford. "Surgical Repair of Atrial Septal Defect", presented by Dr. H. R. Gilmore and Mr. D'Arcy Sutherland.

1959.—February 26: "Industrial Medical Services in South Australia"; speakers, Mr. A. G. Gibbs (Personnel Manager, General Motors-Holden's), and Dr. John Stokes; discussion opened by Dr. D. E. Craven. March 26: clinical meeting, Adelaide Children's Hospital. April 30: Listerian Oration, delivered by Professor C. R. B. Blackburn, entitled "The Liver and the Portal Circulation". May 28: clinical meeting, Queen Victoria Maternity Hospital.

Additional Lectures.

1958.—August 7: by courtesy of The Australasian Association of Psychiatrists (South Australian Branch). September 3: film, by courtesy of the Repatriation General Hospital, Springbank. September 11: by courtesy of Australian Laennec Society (South Australian Branch). October 8: film, by courtesy of the Repatriation General Hospital, Springbank. November 12: film, by courtesy of the Repatriation General Hospital, Springbank.

1959.—March 12: by courtesy of Australian Society of Anæsthetists (South Australian State Committee). April 23: by courtesy of the Australian Laennec Society (South Australian Branch). May 14: by courtesy of the Royal Australasian College of Surgeons (South Australian State Committee).

Attendances at Council and Committee Meetings.

	Council.	Scientific.	Salaries.
BICKFORD, R. N. C.	8	—	—
BONNIN, N. J.	8	1	—
DE CRESPIGNY, R. G. C.	8	1	—
DWYER, J. M.	10	1	1
GIBSON, G. T.	10	—	1
GLYNN, R. McM.[1]	7	—	1
HALLORAN, N.	10	—	—
HEDDLE, R. C.	10	—	—
HUNTER, R.	8	1	1
JEFFRIES, J. S.	8	—	—
JUNGFER, C. C.	10	1	1
MALLEN, L. R.	9	—	1
RIEGER, C. O. F.	10	—	1
THYER, F. L.	9	—	—
VERCO, P. W.	9	1	1
Meetings held up to May 7, 1959	10	1	1

[1] Leave of absence until October 2, 1958.

Membership.

The membership of the Branch as at December 31, 1958, was 936, the number of student associate members being 42.

The deaths of the following members are recorded with regret: Dr. A. P. Cherry, Dr. F. L. Wall, Dr. Paul Ross, Dr. H. F. Wickens and Dr. C. Yeatman.

Appointments and Nominations.

Advisory Council on Health and Medical Services: Dr. L. R. Mallen.

British Medical Association Services Limited: Dr. R. G. C. de Crespigny, Dr. R. M. Glynn, Dr. B. S. Hanson, Dr. L. R. Mallen and Dr. C. O. F. Rieger (Chairman).

British Medical Association, Annual Representative Meeting, Edinburgh, 1959: Dr. R. T. Binns, Dr. A. S. de B. Cocks and Dr. L. A. Wilson.

Central Council of the Association, London: Dr. Myles Formby.

Chiropody Board of South Australia: Dr. Neville Wilson.

Dental Board of South Australia: Dr. Graham Bennett.

Federal Council of the British Medical Association in Australia: Dr. L. R. Mallen and Dr. C. O. F. Rieger.

Royal Flying Doctor Service of Australia (South Australian State Section): Dr. J. M. Dwyer.

Florence Nightingale Memorial Committee of Australia (South Australian Branch): Dr. Dorothy Adams and Dr. Mary Walker.

Medical Board of South Australia: Dr. C. O. F. Rieger.

Mothers and Babies' Health Association: Dr. Nevill Bickford.

Nurses' Board of South Australia: Dr. Thorold Grant.

Old People's Welafre Council of South Australia: Dr. C. Duguid and Dr. J. G. Sleeman.

Rehabilitation Standing Committee (Departmental): Dr. J. R. Barbour.

South Australian Association for Mental Health Inc. (Council): Dr. C. C. Jungfer.

"The Medical Journal of Australia" (Editor's Representative for South Australia): Dr. J. M. McPhie.

The St. John Ambulance Brigade (South Australian District): Dr. H. H. Hurst (Deputy Commissioner).

University Postgraduate Committee in Medicine: Dr. F. L. Thyer, Dr. Ronald Hunter, and the President *ex officio*.

World Medical Association: Dr. L. R. Mallen (Chairman of Council).

Sections Formed for Special Knowledge.

Section of Anæsthetics.

Membership of the section now comprises 42 members.

The following Executive were reelected at the annual general meeting in February for a further twelve months: Chairman, Dr. J. A. Ferris; Vice-Chairman, Dr. M. C. Newland; Past President, Dr. J. H. Stace; Honorary Treasurer, Dr. E. C. Hallett; Honorary Secretary, Dr. D. P. Dineen.

There were six bi-monthly meetings held during the year with an average attendance of 21 members. These meetings were both business and scientific, and seven papers were delivered and discussed by local members and guest speakers.

The Section was honoured in March by a visit from Professor W. Mushin, from the Department of Anæsthesia, Royal Infirmary, Cardiff, who stimulated a busy week of scientific and social activities.

Section of Clinical Medicine.

There are 39 financial members compared with 38 last year.

At the annual general meeting, held on Tuesday, May 13 1958, the following officers were elected: Chairman, Dr. J. S. Covernton; Honorary Secretary-Treasurer, Dr. Robert Hecker; Committee, Dr. S. C. Milazzo, Dr. J. R. Lawrence and Dr. T. H. Beare.

Clinical meetings were held in the Chest Clinic in May, August and November, 1958, and April, 1959, the average attendance being 32 members. Case presentations were of a wide variety, and special note is recorded of two presentations by surgeons at the annual general meeting last May. One meeting was given over to cases of endocrinological interest, and another to cases of infectious diseases.

A disappointing feature is the small number of general practitioners attending the meetings, and the Committee is anxious to adopt measures to overcome this, and to encourage presentation of interesting cases by the outside practitioners themselves. It is proposed in the coming year to increase the representation on the Committee to cover each hospital, including the new Queen Elizabeth and the University Department of Medicine. It is hoped that some meetings in future may be held at the Queen Elizabeth Hospital.

In accordance with a resolution adopted at the annual general meeting, held on May 13, 1958, a gift of £50 was made to the Medical Benevolent Association from the accumulated funds of the Section.

Section of Ophthalmology (South Australian Branch, British Medical Association).

At the annual general meeting of the Section of Ophthalmology (South Australian Branch, British Medical Association), held on March 11, 1958, the following officers were elected for the ensuing year: Chairman, Dr. M. E. Schneider; Vice-Chairman, Dr. F. J. B. Miller; Committeeman, Dr. D. O. Crompton; Honorary Secretary, Dr. A. A. Tye.

Meetings were held in April, July, August, September and November, the average attendance being 15. The Section was privileged to hear several speakers at these meetings. Dr. D. N. Robinson gave a talk with reference to plastic surgery in ophthalmology. Dr. W. C. Woods, Assistant Director of the Radiotherapy Department at the Royal Adelaide Hospital, spoke on "Radiotherapy in Ophthalmology". Dr. D. O. Tonkin spoke on the function of a glaucoma clinic. At the September meeting, Dr. D. O. Crompton was appointed as State Representative on the Council of the Ophthalmological Society of Australia, Dr. M. C. Moore as representative on the Orthoptic Board, and Dr. A. L. Tostevin, Dr. M. C. Moore and Dr. Couper Black as representatives on the Prevention of Blindness Committee.

During the week commencing October 20, 1958, a highly successful Congress was held in Adelaide, and visitors from all States participated in the social and educational activities. Mr. Rycroft, an English ophthalmic surgeon, gave several interesting papers. Many clinical cases of interest were shown throughout the year.

The Oto-Laryngological Society of Australia (South Australian State Section).

The annual general meeting of the Oto-Laryngological Society of Australia (South Australian State Section) was held on March 18, 1958. The existing officers were reelected for another year: Chairman, Dr. A. S. de B. Cocks; Vice-Chairman, Dr. R. H. von der Borch; Committeeman, Dr. P. G. Jay; Secretary-Treasurer, Dr. R. G. Plummer.

Ordinary meetings were held on May 20, July 29, and October 21, 1958.

During November (from Monday 10 to Wednesday 12), Mr. James Crooks, Senior Consulting Surgeon to the Ear, Nose and Throat Department, Great Ormond Street, visited Adelaide and gave several talks to members of the Oto-Laryngological Society of Australia and other members of the profession.

A special general meeting was held on February 10, 1959, to discuss the implications of a proposed plan for the education of the deaf and hard of hearing children in South Australia.

No further meetings were held during the current year.

Affiliated Local Associations of Members.

Northern Medical Association.

Four meetings were held during the year, viz.:

1958.—May 4, at Port Pirie, the speakers being: Mr. B. F. Venner, "Clinical Applications of Serum Electrolytes"; Dr. R. H. Rischbieth, "Headache and Epilepsy". Ten members were present. August 3, at Gladstone, the speakers being: Dr. R. N. Reilly, "Common Nose and Throat Conditions"; Mr. J. R. Barbour, "Painful Conditions of the Feet". Ten members were present. November 2, at Yacka, the speakers being: Mr. Ian Hamilton, "Painful Conditions of the Shoulder"; Dr. R. A. Pellew, "Kidney Diseases". Seven members were present.

1959.—February 1, at Clare, with morning and afternoon sessions. The speakers were: Dr. C. B. Stangster, "Cerebral Vascular Diseases"; Mr. O. W. Leitch, "Odd Conditions of the Hand"; Dr. E. B. Sims, "Abdominal Pain in Children"; Dr. G. W. E. Aitken, "Cæsarean Section". Eleven members were present.

The office-bearers are: President, Dr. V. W. Potter; Vice-President, Dr. N. F. Denton; Honorary Secretary, Dr. R. T. Davidson.

Upper Murray Medical Association.

Officers elected at the annual general meeting, held on February 22, 1958, were as follows: President, Dr. J. G. Wilson (Renmark); Vice-President, Dr. R. L. Miller (Waikerie); Honorary Secretary, Dr. G. Hasenohr (Barmera). Following Dr. Wilson's departure from the district, Dr. Miller became President for the remainder of the year.

Three post-graduate week-ends were held during the year, as follows:

1958.—May 3, at Renmark: visiting lecturers were Dr. R. M. MacIntosh, Dr. D. N. Robinson and Dr. S. C. Milazzo. August 2, at Barmera: visiting lecturers were Dr. H. E. Pellew, Dr. J. P. Maddern and Dr. Robert Hecker; November 1, at Berri: visiting lecturers were Dr. J. V. Gordon, Dr. Rodney White and Dr. L. J. Rice.

Salisbury and Elizabeth Medical Association.

The inaugural meeting was held on February 12, 1959, when the following officers were elected: President, Dr.

F. E. Trembath; Secretary-Treasurer, Dr. V. M. Newland; Committee members, Dr. V. Hart and Dr. E. D. Richards.

South-Eastern Medical Association.

Five meetings were held during the year.

On August 2, 1958, at Penola, a clinical meeting was held, and after dinner Dr. Kay spoke on "The Management of Heart Failure". On October 18, 1958, at Mt. Gambier, Mr. H. D. Sutherland spoke on "Traumatic Injuries of the Chest". On February 28, 1959, at Mt. Gambier, a clinical meeting was held, and after dinner the State President of the British Medical Association (Dr. C. C. Jungfer) discussed the more recent activities of the Branch, and Dr. R. Greenlees discussed the aims and objects of The Australian College of General Practitioners, South Australian Faculty. On May 2, 1959, a clinical meeting was held at Naracoorte, and Dr. Pincus Taft spoke on "Recent Advances in Endocrinology".

At the annual general meeting the following officers were elected: President, Dr. D. K. Kumnick; Vice-President, Dr. J. S. Jeffries; Secretary-Treasurer, Dr. I. G. Campbell; Committee members, Dr. C. H. Leeson and Dr. R. H. Jarvis.

The annual refresher course was held at Mt. Gambier on July 5, 1958, and visiting speakers were: Mr. A. G. Campbell, "Treatment of Burns"; Dr. V. Bockner, "Post-Partum Problems"; Dr. B. S. Hetzel, "Intravenous Therapy".

There are 34 financial members of the Association, and the average attendance at meetings, excluding visitors, has been 18.

Yorke Peninsula Medical Association.

During the year ending June, 1959, four post-graduate week-end lectures have ben held and well attended by 14 members. These have been held at Wallaroo and more distant centres.

Wallaroo, and in addition this year Kadina, has supplied 50 to 60 pints of blood on donor days to the Red Cross Blood Bank, not only to enable serum to be manufactured, but also to keep our donors and new members interested in such needs. In the near future we hope to add Moonta to the panel.

On May 31, a meeting will be held for the election of officers of the Association for the ensuing year. Present officer-bearers are as follows: President, Dr. P. J. Reilly; Immediate Past President, Dr. F. L. Thyer; Secretary-Treasurer, Dr. G. J. Smibert; Committee members, Dr. W. T. Chappell and Dr. R. Barnes.

Overseas Subscription Rate Payable to the Parent Association.

The Council of the London Office is submitting a recommendation to the Annual Representative Meeting, to be held at Edinburgh in July next, that the standard rate of subscription payable by members of the Association residing outside the United Kingdom be raised from two to three guineas. The reason for this is the constantly rising costs of maintaining the Association's essential services and to enable it to carry on its expanding activities.

If this recommendation is approved by the Annual Representative Meeting, the Australian Branches will be required to pay an additional amount of £A1 14s. 5d. for each member on the membership list to the London Office as from January 1, 1960.

Revival of Medico-Legal Society.

Following the scientific meeting on the subject of "Medical Secrecy" in July, 1958, in view of the interest shown by members of the medical and legal professions in this subject, steps were taken to convene a meeting of those interested in re-forming the Society. The Society was previously disbanded at the beginning of World War II.

The initial meeting was held in the Reception Room at "Newland House" on May 4, 1959, when a very representative number of both professions attended. It was unanimously decided to revive the Society, and to meet quarterly on future occasions to discuss topics of mutual interest to both professions. Mr. Justice Reed was elected President of the Society, and Dr. C. C. Jungfer and Mr. J. L. Travers, Vice-Presidents respectively. A committee of five members from both the medical and legal professions was also appointed, the medical representatives being as follows: Dr. J. M. Dwyer, Professor J. S. Robertson, Dr. B. J. Shea, Dr. J. G. Sleeman and Dr. Arthur Welch.

Medical Certification.

Despite repeated notices in the monthly circular indicating the guiding principles of certification, complaints have been received throughout the year from both private industry and Government departments. The commonest fault is ante-dating certificates.

Council is very concerned about the damage done to our profession as a whole by the issue of improper certificates. It must be stressed that any certificate which is misleading or false can be investigated by the Medical Board, which has power to recommend that the name of the offending practitioner be erased from the Register.

Council again urges members to exercise particular care in issuing certificates to any person. A certificate must not be issued unless the person has been actually attended during the course of the illness. Certificates must be given only on medical grounds based on the practitioner's personal knowledge of the health and physical condition as ascertained at the time the certificate is issued.

There is provision in the Act for sick pay to be claimed by the patient making a statutory declaration. Consequently there is absolutely no occasion for ante-dated certificates.

Industrial Medical Services.

In view of the rapid expansion of industry in South Australia, the February scientific meeting of the Branch was devoted to the subject of "Industrial Medical Services". A number of invitations to attend this meeting were issued to leading industrialists and other interested groups.

The meeting aroused considerable interest among doctors and industrialists, and, subsequently, a communication was received by Council from the President of the Metal Industries Association of South Australia, suggesting the establishment of a roster of general practitioners so as to ensure that industrial accidents received prompt attention at all times.

Recognizing the importance of developing an emergency medical service for industry, Council has asked metropolitan groups to consider this problem and to submit their views on this proposal.

Establishment of an Emergency Accident Service.

Following a suggestion made at a previous scientific meeting, in December, 1958, Council launched a pilot scheme whereby a team of surgeons is available to go to the assistance of country doctors in an emergency. The following conditions apply:

(a) The request for the supply of the service must come from the country practitioner, who is left perfectly free, however, to make his own arrangements if he so wishes.

(b) Following the initial service, the patient would remain in the country hospital under the post-operative care of the general practitioner, excepting under unusual circumstances.

(c) Transport for the surgical team is provided by the St. John Ambulance Brigade.

(d) The name of the surgeon on duty can be obtained by ringing the St. John Ambulance Brigade, LU 5184, at any time day or night.

The Royal Flying Doctor Service of Australia (South Australian Section) has also expressed its willingness to supply air transport in outback areas, when the necessity arises.

A number of emergency services have been provided since the inception of the service.

It is hoped by Council that this arrangement will make specialist surgical help more readily available to country doctors, and that it will enable more patients to remain in their own district hospitals.

National Health Act.

During the year the Federal Council sought the opinion of the Branches and the various specialist bodies on the question of anomalies in the existing schedule of benefits, for later submission to the Government. A Special Subcommittee was appointed for the purpose of preparing a revised schedule, and this report was later presented to the Minister for Health, and referred by him to the inaugural meeting of the Commonwealth Health Insurance Council. It is universally recognized that the schedule of benefits requires to be amended in many respects, and it is hoped that the Government will accept the advice which has been given.

SOUTH AUSTRALIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION (INCORPORATED)

Balance Sheet as at December 31, 1958.

Liabilities.	£ s. d.	£ s. d.	Assets.	£ s. d.	£ s. d.
Sundry Creditors		1,704 5 1	*Fixed Assets at Cost, less* Depreciation:		
General Fund:			*Furniture and Plant*	1,719 4 6	
Balance as at January 1, 1958	11,554 6 0		Delineascope and Projector	4 6 8	
Add Net Surplus for year	1,140 19 11		Lister Medals	2 0 0	
		12,695 5 11			1,725 11 2
			Current Assets:		
			British Medical Hall Company Limited—Shares at Cost	4,217 10 0	
			Australasian Medical Publishing Company Limited — 6¼% *Debentures*	3,530 0 0	
			Advances not converted	91 13 1	
			British Medical Association Services Limited Shares	500 0 0	
					8,339 3 1
			Stocks on Hand	227 8 0	
			Sundry Debtors	3,518 5 8	
					3,745 13 8
			Cash at Bankers:		
			National Bank of Australia	42 0 2	
			Commonwealth Saving Bank	157 8 10	
			Savings Bank of South Australia	373 5 7	
			Savings Bank Library Account	1 19 6	
			Cash in Hand	14 9 0	
					589 3 1
		£14,399 11 0			£14,399 11 0

Special Funds and Investments.

	£ s. d.	£ s. d.		£ s. d.	£ s. d.
Listerian Oration Fund:			Listerian Oration Investments:		
Balance, January 1, 1958	388 12 4		*E.T.S.A. Debentures*	310 0 0	
Add Net Income	18 3 5		Savings Bank of South Australia	54 19 9	
	406 15 9				364 19 9
Less Oration Expenses	41 16 0				
		364 19 9			
Frank S. Hone Memorial Fund:			Frank S. Hone Memorial Fund *Investments:*		
Balance, January 1, 1958	738 17 2		Commonwealth Bonds 3½%, 1959	50 0 0	
Add Interest	22 8 7		South Australian Gas Company Debentures	300 0 0	
	761 5 9		*E.T.S.A. Debentures*	250 0 0	
Less Prize	15 15 0		Savings Bank of South Australia	145 10 9	
		745 10 9			745 10 9
Trent Champion de Crespigny Memorial Fund:			Trent Champion de Crespigny *Memorial Fund:*		
Balance, January 1, 1958	295 11 0		Savings Bank of South Australia		304 3 1
Add Interest	8 12 1				
		304 3 1			
British Medical Hall Building Fund:			British Medical Hall Building Fund:		
Balance, January 1, 1958	891 7 6		*Commonwealth Bonds 3½%, 1960*	200 0 0	
Add Interest and Donations	3,457 6 5		Savings Bank of South Australia	2,136 11 11	
		4,348 13 11	Commonwealth Savings Bank	1,691 17 0	
			Commonwealth Bank General Funds	320 5 0	
					4,348 13 11
		£5,763 7 6			£5763 7 6

F. C. W. Dossin, Secretary. J. M. Dwyer, Hon. Treasurer.

We hereby report that we have examined the Books and Accounts of the South Australian Branch of the British Medical Association Incorporated for the year ended December 31, 1958. In our opinion the above Balance Sheet, together with the Statements of the Special Funds, are properly drawn up so as to exhibit a true and correct view of the affairs of the Branch, as at the above date, according to the best of our information, the explanations given to us, and as shown by the Books produced.

Adelaide, June 3, 1959.

Annells, Tilley, Hunwick and Co.,
Chartered Accountants (Aust.).

Income and Expenditure Account for the year ended December 31, 1958.

1957 £		£ s. d.	1957 £		£ s. d.	£ s. d.
15	To Audit Fee	19 19 0	8,815	By Gross Subscriptions		9,369 4 0
6	„ Advertising	2 13 9	6,662	City	7,177 19 0	
201	„ Depreciation	191 10 2	2,109	Country	2,146 15 6	
170	„ Entertainment	149 5 9	42	Students	44 9 6	
344	„ General Office Expenses	649 13 6	3,512	*Less* Deductions		4,012 11 9
25	„ Legal Expenses	8 18 6	1,434	B.M.A., London	1,494 11 9	
454	„ Postages	466 0 9	395	M.J.A.	459 10 0	
2,503	„ Secretariat	2,106 7 0	600	Library	939 15 0	
480	„ Printing and Stationery	573 3 3	1,082	Federal Council	1,118 15 0	
48	„ Telephone	48 0 8				
1,272	„ Net Surplus for Year	1,140 19 11		Net Subscriptions		5,356 12 3
		£5,356 12 3				£5,356 12 3

In August it was announced the the Government intended to guarantee special funds to be set up by voluntary health organizations so as to provide both Commonwealth and fund benefits for those who had previously been excluded by reason of preexisting and chronic conditions. Such special funds were established as from January 1, 1959. However, it was later ascertained that the Government had refused to recognize many of the smaller private hospitals for the purpose of the increased hospital benefits, and many aged and infirm patients in these institutions were debarred from receiving benefits from these special accounts. In support of the principle that these persons should be able to receive increased benefits in exactly the same way as other members of the community, the Federal Council later informed the Minister that it was considered that fund benefit should be payable in relation to the medical condition of the contributor, and not to the hospital in which he occupied a bed.

The Organization of the Medical Profession in Australia.

Whilst there are many sentimental reasons why membership of the British Medical Association appeals to Australian doctors, it is becoming accepted that the profession in Australia should have its own medical association independent of, but affiliated with, the British Medical Association. There is no doubt that the profession in Australia has grown up to the extent that it is now both large and strong enough to be self-supporting. There is also no doubt that it will eventually follow the pattern which has been set previously by the Canadian and South African Associations respectively.

The various advantages and disadvantages of the present arrangement have been placed before Branch Councils by the Federal Council on several occasions throughout the past year. At the March meeting of the Federal Council, and at the request of the various Branches in Australia, it was therefore decided to take the necessary steps to investigate the possibility of forming a Medical Association of Australia.

It is emphasized, however, that the drawing up of a constitution for an Australian Medical Association would possibly take the best part of two years to accomplish.

The Erection of Additional Office Accommodation and the Provision of a Memorial Hall on the Property of the Branch.

A special Building Committee, under the chairmanship of Sir Henry Newland, was appointed by the Council during the year to discuss with the architect the question of plans involving the provision of additional office accommodation and the erection of a Memorial Hall on the Brougham Place property.

At a meeting of the Council held on June 3, 1959, the recommendations of the Building Committee were adopted, and a tender amounting to £41,566 10s. for the completion of the project was accepted. It is estimated that the additions will be completed in nine months. The price includes the provision of a very fine clubroom for the use of members, and the enlargement of one existing professional suite.

Arrangements have been made with a lending institution for a maximum advance of up to £35,000 so that the work may be put in hand as soon as possible. However, the contribution of a substantial portion of the contract price by members will lessen the amount requiring to be paid by way of interest and reduction of capital, and so permit the Branch to be relieved of its financial obligation at a much earlier date.

The question of raising the necessary finance has been entrusted to the Memorial Hall Committee, and a brochure setting out full details of this very desirable project is being prepared for circulation to members.

Australasian Medical Congress (B.M.A.) Eleventh Session.

The next session of the Australasian Medical Congress will be held in Adelaide in (May) 1962, and the Federal Council has approved of the nomination of Dr. C. O. F. Rieger as President of the Eleventh Session. The Honorary Secretary is Dr. Robert Hecker. A meeting of the Council held on May 7, 1959, in accordance with the usual custom, constituted the first General Committee, and proceeded with the appointment of various members to the Executive Committee.

The first meeting of the Executive Committee will be held at an early date.

British Medical Association Services Limited.

A report received from the Directors of British Medical Association Services Limited indicates that the income received by the company as a result of its activities throughout the first year of its existence has been most gratifying.

The full support of members will enable this company (which is owned and controlled by the South Australian Branch of the British Medical Association) to expand its activities and materially assist the Branch in proceeding with future building plans.

Honorary Life Membership.

The congratulations of the Council were extended to Dr. L. J. Dunstone and Dr. L. W. Jeffries, who completed 50 years' continuous membership of the Association during the year and thus became Honorary Life Members.

Federal Council of the British Medical Association in Australia.

The Federal Council met in Melbourne on September 4, 1958, and in Sydney on March 21, 1959. The Branch was represented on these occasions by Dr. L. R. Mallen and Dr. C. O. F. Rieger.

Reports of these meetings were later published in The Medical Journal of Australia.

Frank S. Hone Memorial Prize.

The prize awarded on the results of the 1958 examination for the degrees of bachelor of medicine and bachelor of surgery was won by Douglas John Barlow.

Honours and Awards.

The Council extends its congratulations to Dr. L. R. Mallen on his appointment as Chairman of Council of the World Medical Association, and also to Dr. F. K. Mugford, who has been promoted to the Grade of Knight of Grace, and Dr. R. F. Matters, who has received promotion to Grade of Officer in the Venerable Order of St. John of Jerusalem.

Conclusion.

During the past year Council has concerned itself with many matters concerning the welfare of the community and the welfare of the members of this Branch.

Although it may appear to some members that the threat of a nationalized medical profession in Australia has lessened, this is by no means so. There are still strong

forces at work demanding that the freedom of our profession be sacrificed to ideological plans which give little consideration to standards of medical care.

If we are to remain free, we must be certain that our standard of service keeps pace with modern advances in medicine, and we must ensure that relationships with our colleagues and with our patients are as harmonious as is possible in any human society.

C. C. JUNGFER,
President.

FINANCIAL STATEMENT.

The financial statement was presented by the Honorary Treasurer, Dr. J. M. Dwyer, and adopted.

ELECTION OF OFFICE-BEARERS.

There being no other nomination, Dr. Jungfer declared Dr. G. T. Gibson elected to the office of President for the ensuing year, and invested him with the badge of office. Dr. Gibson thanked the members for his election.

Dr. Gibson then announced the following office-bearers for the ensuing year:

Vice-President: Dr. R. G. C. de Crespigny.

Honorary Treasurer: Dr. J. M. Dwyer.

Honorary Medical Secretary: Dr. Robert Hecker.

Members of Council: Group A (metropolitan), Dr. E. P. Cherry, Dr. I. S. Magarey, Dr. H. R. Oaten. Group B (country), no nomination received by the closing date.

Messrs. Annells, Tilley, Hunwick and Company were appointed auditors for the ensuing year.

RETIRING MEMBERS OF COUNCIL.

A vote of thanks was passed to the retiring members of Council, Dr. R. N. C. Bickford, Dr. R. M. Glynn, Dr. F. L. Thyer, Dr. P. W. Verco and Dr. R. Hunter.

RETIRING PRESIDENT'S ADDRESS.

Dr. C. C. Jungfer delivered his retiring president's address (see page 585), after which a vote of thanks was passed to him.

THE AUSTRALIAN SOCIETY OF ALLERGISTS (B.M.A.).

ANNUAL MEETING.

THE sixth annual meeting of the Australian Society of Allergists (B.M.A.) was held on October 23 and 24, 1958, at Melbourne.

Election of President.

DR. BERNARD RILEY, of Sydney, was elected President of the Society for the year 1958-1959.

Alteration of the Rules of the Society.

An alteration in the rules of the society was adopted.

Bronchodilator Therapy and Adrenaline-Fastness.

DR. BRYAN GANDEVIA (Melbourne) read a paper entitled "Bronchodilator Therapy and Adrenaline-Fastness". He said that simple tests of ventilatory capacity based on a single forced expiration formed the best method of assessing objectively the effects of a bronchodilator drug. Assessment might take the form of a series of "acute experiments", when repeated tests of ventilatory capacity were made over an appropriate period after the drug had been given, or of a clinical trial in which patients were given either the trial drug and/or a placebo and assessed at appropriate intervals. Studies of the latter type had, in summary, suggested the value of the following procedures: the administration of choline theophyllinate, 200 milligrammes every six hours (or "Theodrox", one tablet every six hours) combined with phenobarbitone, 20 milligrammes twice or thrice daily; the exhibition of ephedrine, a quarter to a half grain every four to six hours, but repeated in half to one hour if necessary, for not more than three days at a time if used continuously (tolerance developed after this time unless there was a further increase in dosage); the use of aminophylline suppositories (0·5 gramme) which were effective if inserted at night. Intramuscular injections of aminophylline and particularly certain aminophylline-like proprietary preparations for oral ingestion were relatively and in some cases wholly ineffective. It was convenient to alternate the courses of ephedrine and theophylline compounds, changing from one to the other twice a week. Aminophylline suppositories were particularly useful to cover the period before, during and after surgical operations, when, particularly in the emphysematous patient, maximum bronchodilatation was necessary.

Dr. Gandevia went on to say that adrenaline fastness, which occurred as a rule in patients in status asthmaticus, was commonly regarded as a pharmacological phenomenon; but there was evidence to indicate that it was due at least in part to mechanical factors. Patients in whom a severe attack of asthma was precipitated by the experimental inhalation of allergens to which they were sensitive responded very rapidly to adrenaline, and so did patients who took adrenaline or adrenaline-like substances at the very earliest stage of a naturally occurring attack. However, once the attack had been present for some hours, the response to adrenaline, as measured by tests of ventilatory capacity, was relatively small. If the patient's response to adrenaline was tested on subsequent days as the severity of wheeze was steadily diminishing, the response to adrenaline increased progressively up to a certain maximum. Thereafter, with further relief of the patient's initial state of wheeze, the response to adrenaline diminished so that when the patient had no wheeze at all the response to adrenaline was nil. Those findings were independent of dose or route of administration of adrenaline, and applied with equal force to certain other drugs, notably atropine and aminophylline, although the effect of the two last-mentioned drugs given alone was usually somewhat less than would be expected from adrenaline. It was inferred from those findings that, whatever the factors which were responsible for the initial stages of an asthmatic attack, they were reversed or eliminated by the action of adrenaline, but that some additional factor or factors not affected by adrenaline came into play when the attack had been in progress for some length of time. The most likely factor at that stage was the secretion of tenacious mucus.

Dr. Gandevia showed bronchograms to illustrate a further mechanical factor operative in patients with wheeze in addition to established structural emphysema. He said that in some of those cases, portion of the bronchial tree collapsed almost completely because of the high pressure difference between the outside and inside of the bronchial wall over a short segment of the main bronchus just after it had left the support of the lung tissue. While bronchodilator drugs might produce some improvement in expiratory flow in those circumstances, that phenomenon was essentially irreversible by drug therapy. It was in those circumstances that some expiratory resistance at the mouth might be helpful in keeping the major bronchial pathways open. It was also in those circumstances that it was important to teach patients to breathe in a quiet, relaxed fashion; intrapleural pressures were kept to a minimum, and thus the tendency for the bronchial wall to collapse was also reduced.

Dr. Gandevia said in conclusion that adrenaline-fastness could be adequately explained without postulating pharmacological "tolerance", although the possibility that that could occur was not excluded.

New Therapeutic Measures in Asthma.

DR. V. BRISTOW (Melbourne) discussed three new drugs for use in the treatment of asthma—a bronchodilator and two new steroids. He said that the bronchodilator was ethylnoradrenaline, marketed in America as "Bronkephrine". It differed from adrenaline in having the side chain lengthened to four carbon atoms, and in lacking the methyl group on the amine radical. It was weight for weight about one-tenth as effective as adrenaline, but that increased dosage was well within safety limits. A dose of one millilitre of the 0·2% solution was at least as effective as 10 minims of 1:1000 adrenaline tartrate, and the side-effects were much less marked. The tremor and palpitation usually associated with adrenaline were rarely noticed, and when observed there was always a drop in both systolic and diastolic blood pressure. Dr. Bristow said that he had used the drug on more than 100 occasions and there had been only one case of mild shock and collapse. He thought that it was much safer than adrenaline tartrate and quite as effective. He hoped that it would soon be freely available in Australia.

Dr. Bristow went on to say that the steroids concerned were delta 1, 6 alpha-methyl-hydrocortisone, sold under the name of "Medrol", and 9 alpha fluoro 16 alpha-hydroxy-

prednisolone, or "Triamcinolone", marketed as "Ledercort" or "Kenacort". Both drugs were two to four times as potent as prednisone or prednisolone, and apparently had no sodium or fluid retaining properties. Indeed, "Triamcinolone" was criticized in some articles as a possible cause of excessive sodium excretion and dehydration. Both steroids depressed appetite, and "Triamcinolone" might cause undue dyspepsia, with a general depression of the central nervous system and even muscular weakness.

Dr. Bristow said that he had had one patient who combined hypertension and chronic asthma, whose blood pressure dropped adequately when "Triamcinolone" therapy was begun, but in whom it produced severe dyspepsia. When a change to "Medrol" was made, the dyspepsia disappeared without any rise in blood pressure. There was certainly a use for those new steroids for some patients, particularly those requiring long-term treatment, and of the three he tended to favour "Medrol".

Progress Report on a Pollen Count.

Dr. C. Sands (Canberra) gave a progress report on a pollen count. He said that it was now two years since he had introduced the work to the Society. At that time, his diagram had progressed for nine months. He was now into his third year of observation. At that time, he had asked members to give him their ideas on carrying on the work, and their response had been good. Once again he was asking them for their cooperation and suggestions.

Dr. Sands went on to say that he had been making a daily count of the pollen fall-out from the air and recording what appeared to him to be the relevant weather variations. That initial period caught the tail end of one season and all the next season. It so happened that those seasons were extremely wet in south-east Australia, and the pollen production was proportionately high (frequently 200 per cubic centimetre of air, and rising as high as 900). The next season (1957) there was very little rain. For instance, the December-January period, the latter part of February, the latter part of March and June had almost no rain, and the practical result of that was that the pollen fall-out for that year was very slight. In fact, in the late spring and autumn, it was rare for the pollen fall-out to exceed 25 pollens per cubic centimetre of air, and frequently it was much less than that. Nevertheless, symptoms occurred among the population and the symptoms were not always in agreement with the pollen fall-out. That finding was not entirely unexpected, and would be the subject of comment later. Referring to the year 1958, Dr. Sands said that there had been frequent slight showers of rain, which had been sufficient to produce a very good growth of grass. In consequence, he was expecting a heavy pollen season in spring; but the pollen season for the grasses did not begin until the middle of October, and so he could not anticipate results yet.

Dr. Sands then said that early in the pollen count he had realized that it would be desirable to have some precise information as to the daily symptoms suffered by a number of people. Until recently, he had been recording symptoms as he had observed them amongst companions and people in the streets and relating those observations to the pollen count. That was helpful, but not sufficiently precise, so he had enlisted the assistance of statistically-minded people, and they had devised a method of survey for him. Although that survey in the beginning was, to his mind, merely to be a relation of symptoms of allergic people to the pollen fall-out, he soon realized that the survey being suggested by the statistics people covered a much wider field and that it was becoming more and more elaborate from day to day. He had therefore decided to call it straight out "The Survey of the Common Cold". In order to carry out the survey, an enthusiastic band of women helpers had been efficiently organized by Mrs. A. B. Hill, of Canberra. That band of helpers was collecting subjects from 250 houses scattered at random in Canberra, and he hoped that that would produce about 1000 separate people under observation. Those people were being asked to give answers daily to five questions, and it was the applicability of those questions that he wished to discuss at the meeting. Those present would realize that the organization required to obtain those answers to the questions was considerable, and involved much work on the part of a number of voluntary helpers. He could not speak too highly of those voluntary helpers, and of the original organization put into their work. To keep a large number of people daily answering throughout a whole year questions which to them were not particularly interesting, was quite a problem. The five questions were: (i) whether there was excessive sneezing—outbursts of sneezing more than twice in succession, not just the isolated sneeze; (ii) whether there was excessive watering or blocking of the nose; (iii) whether there were coughing fits (*a*) when lying down and (*b*) at other times; (iv) whether asthma was present; (v) whether there was any increase in symptoms of eczema or hives. Excessive sneezing and watering of the nose were common to both the infectious cold and the allergic cold. It was hoped, when a history of the different people had been examined, to be able to determine which was likely to be the type from which they were suffering. Coughing fits when lying down were frequently indicative of early asthma, or what one might call pre-asthma, especially in children. When they were coughing during the day, it was likely to be an infectious cold unless the asthma was a more definite type. Asthma, of course, was for those who were definitely allergic. The question on eczema and hives had been added in an attempt to find what was the seasonal incidence of those conditions. A column had also been added, in which the subjects were asked to tabulate any days away from work or school or other regular occupation. Dr. Sands said that when all that information was obtained, he anticipated that a long period would be required to digest the answers. Actually that digestion was being carried out continuously during the survey, but there would still be much required when the survey was finished. He hoped that by the next annual meeting he would be able to give some results as to the relationship of pollen count to the symptoms suffered. He had noticed that a large pollen fall-out over some period, especially early spring and late autumn, did not produce a corresponding response in symptoms. Early in the survey, he had realized that they were obtaining much more on their slides than pollens. Much of the material was just plain dust, and presumably might act as an irritant, but was not an allergic factor; but also they obtained much in the way of hyphæ and spores of the different moulds. Those moulds were being discussed by Dr. D. Cross, but his own observations suggested that there was a big production of those mould spores in the periods that he had mentioned—late summer and early spring. He thought that the moulds might be the cause of the high instance of symptoms at those periods. Actually, he was endeavouring to interest certain people in making a survey for the moulds in south-east Australia, and if he could persuade them to do so, then the problem of the allergic condition in south-east Australia might show a definite rhythm with the production of the pollens *plus* the spores.

Clinical Experience with Moulds.

Dr. D. Cross (Sydney), by way of introducing the subject of moulds in allergy, discussed briefly the composition of the atmosphere as it impinged upon human beings. He said that part of the atmosphere was composed of the organized plant and animal material. The plant material of organized nature was largely termed air spora. That was composed of the spora called pollen grains of the higher plants, the spores of Gymnosperms (pines, etc.), Pteridophyta (ferns, etc.) and finally of lower plants such as the mosses, liverworts, fungi and bacteria. He dealt especially with the spores of fungi, and particularly those of the so-called moulds as distinct from the higher fungi. He mentioned the nature of spores in the life cycle of the moulds, and the chief air-borne types of moulds of importance in human allergy were discussed with their relationships to other fungi. He submitted some preliminary observations in the testing and treatment of some 200 recent patients, and said that a further analysis of the remainder of patients examined and treated in the last 12 months would be presented later. He demonstrated a new method for accurate collection of data relating to air spora, and some cultures of the common moulds.

In conclusion, Dr. Cross stressed the present lack of knowledge of Australian air-borne moulds and their allergenic effects, and appealed for research work in that field, so that patients might have the benefit of better understanding and treatment.

"Inadvertant Anaphylaxis."

Dr. S. Brand (Melbourne) discussed inadvertent anaphylaxis. He said that the term anaphylaxis usually denoted generalized constitutional reactions experimentally produced, or similar reactions in man following the introduction of excessive amounts of antigen, usually by parenteral injection. Local reactions also occurred, and a variety of insults might determine their localization. After a sublethal shocking dose, tolerance to the antigen developed, and desensitization procedures were based on

that phenomenon. The initial injection of a second course of therapy with an antigenic substance was the dangerous one, especially if it was given intravenously. Histamines, heparins, serotonin and other chemical mediators were involved, and antagonistic drugs might be therapeutic agents. Clinically, acute anaphylactic shock differed from acute anaphylaxis, in that extreme hypotensive circulatory failure predominated in the former, whilst localized shock-organ response with bronchospasm, urticaria, angio-œdema, etc., predominated in the latter. Immediate application of a tourniquet above the site of the injected antigen, the injection of 0·3 millilitre of 1:1000 adrenaline solution beneath the site and the adoption of the head-low position were emergency measures often neglected. In severely shocked patients, adrenaline could be dangerous; replacement of blood volume with serum and pressor drugs—e.g., noradrenaline—to maintain blood pressure, was indicated. The intravenous administration of hydrocortisone and antihistamines was also useful, and should be continued for seven days or so. Delayed and protracted anaphylaxis might occur. Dr. Brand said that the commonest causes of anaphylaxis were (i) parenteral drug and serum therapy and (ii) desensitization and skin-testing procedures. An allergic history or symptoms of a previous sensitivity reaction called for added care. Scratch tests would probably produce positive reactions in cases of unusual sensitivity likely to result in anaphylactic shock.

Prevention of Anaphylactic Shock in the Guinea-Pig.

DR. S. WIENER (Melbourne) discussed the prevention of anaphylactic shock in the guinea-pig. He said that whenever a foreign protein, and particularly horse serum, was injected into man, the risk of anaphylactic shock was present. Although various sensitivity tests had been designed to reduce that risk, they were not always reliable; moreover, in the case of a snake-bite requiring antivenene, there might not be sufficient time to perform them. Experiments had been carried out to study the effect of various substances for their ability to prevent anaphylactic shock. In work done with guinea-pigs, it was found that sensitization with horse serum was not a reliable method for the production of experimental anaphylaxis. However, animals which had received one dose of different antigens containing diphtheria toxoid developed a high degree of sensitization, and anaphylactic shock could be produced regularly by the intracardial injection of purified diphtheria toxoid 6 to 12 weeks later. The antigens used for sensitization included triple antigen, combined diphtheria and tetanus toxoids, and purified diphtheria toxoid adsorbed on aluminium phosphate (P.T.A.P.). The percentage of animals which died could be controlled by varying the amount of toxoid in the "shocking" dose. With less than 5 Lf of diphtheria toxoid, no shock was produced, whilst with 40 Lf or more of toxoid 100% of animals died from anaphylactic shock. Within half a minute to three minutes after the injection of a minimum lethal "shocking" dose, the animals showed the following signs: scratching of the face, explosive expiratory rasping sounds, acute dyspnœa, restlessness, weakness and discharge of urine. Death, due to asphyxia, occurred in two to five minutes after the injection of antigen. The lungs were pale and grossly emphysematous, and floated on ether.

Dr. Wiener said that over 500 guinea-pigs weighing 500 to 650 grammes had been used in the experiments. Six to 12 weeks after they had been sensitized to diphtheria toxoid, 40 to 80 Lf of purified diphtheria toxoid were injected intracardially. Five milligrammes of "Antistine", when injected intraperitoneally 15 minutes before the "shocking" dose, prevented death from anaphylactic shock in 100% of animals. Five hours after the injection of that dose of "Antistine", no protection was observed. With an initial dose of 25 milligrammes of "Antistine", protection was still observed five hours later. When "Antistine" was injected together with the antigen, at least one milligramme had to be given to prevent symptoms of anaphylaxis. With smaller amounts of "Antistine", anaphylactic shock was delayed, and death occurred in some of the animals. No protection was observed when less than 0·2 milligramme of "Antistine" was used. In animals which died from delayed shock 30 to 60 minutes after the injection of a mixture of antigen and 0·5 milligramme of "Antistine", death was not preceded by dyspnœa, and the lungs were collapsed and did not present the typical pale emphysematous appearance usually observed in guinea-pigs which died from acute anaphylactic shock within five minutes after the injection of antigen.

Dr. Wiener went on to say that a number of other substances had been tested. Adrenaline hydrochloride in a dose of 0·002 milligramme when injected together with one lethal "shocking" dose, prevented death in 12 out of 13 animals. Once symptoms of anaphylaxis had developed, adrenaline did not save the animals. Ten to 20 units of ACTH injected one to three hours before the "shocking" dose did not prevent anaphylaxis. A similar absence of a protective effect was observed when atropine, amphetamine and piperoxane were used. Some protection was observed with aminophylline and procaine, urethane or ether anæsthesia. Animals which had survived an injection of the "shocking" dose were not regularly "desensitized" when tested again 24 hours later. Desensitization was observed in animals which had originally survived two or more lethal doses under an antihistamine cover, and particularly in those which had shown non-fatal symptoms of anaphylaxis. Of animals which had survived only one lethal dose of antigen under an antihistamine cover, 70% died when again injected with a similar amount of antigen 24 hours later.

Dr. Wiener pointed out that the observations showed that relatively large doses of "Antistine" (two to five milligrammes per kilogram) would prevent anaphylactic shock in the guinea-pig. He suggested that for the prevention of anaphylactic shock in man, 100 to 200 milligrams of "Antistine" be injected before the injection of serum. Similarly, a few minims of adrenaline injected subcutaneously with the serum could be expected to confer a significant degree of protection against anaphylactic shock.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

EMBARGO ON DOGS.[1]

[From the *Australasian Medical Gazette*, October, 1883.]

THE Government has issued a proclamation forbidding the importation of dogs to N.S. Wales, the present law not allowing the imposition of quarantine regulations as to these animals. This, in view of the terrible consequences of the introduction of hydrophobia is only prudent, until at all events such a change is made in the law as enforces a sufficient period of isolation prior to their release in the colony.

Correspondence.

CANCER OF THE LUNG.

SIR: South Australia holds the key, if it can be found, to the cause of the increase in cancer of the lung. My figures for the seven successive thousands of post-mortems at the (Royal) Adelaide Hospital between 1920 and 1948 are as follows: 2, 3, 10, 18, 22, 28 and 30. The increase, it will be seen, began in the 1930's. Allowing for an incubation period of about ten years or more, what predisposing cause began to operate more and more about 1920 and the end of the first World War? As the increase in cancer of the lung began in Britain and in the United States of America about the same time, the factor must be common to the three. Wood fires are used in Adelaide, so it cannot be the smoke from coal fires. Adelaide became no more suddenly urbanized about 1920 than it had been in 1900. It has increased in size greatly during the last twenty years, but it cannot be considered an industrial or crowded city—it is, in fact, a garden city. Urbanization cannot be considered a reasonable cause. Before the first World War, bitumenized and tarred roads were few. They only began to increase extensively in the 1930's, but the predisposing cause had been operating for ten years at least before this. It is possible, of course, that bitumenized roads may now be contributing to the increase. In the 1920's motor vehicles were becoming more generally used—I bought one myself in the middle 1920's. Men use them more than women, but I do not think they contribute to the increase. It is

[1] From the original in the Mitchell Library, Sydney.

unreasonable to attribute the increase to more telephones being used, to electricity replacing gas, to more tinned foods. Before the first war, men smoked pipes and some smoked cigars—they had done so for fifty years and more before, and some were heavy smokers. A few smoked cigarettes. During the 1914-1919 war, comfort funds supplied the troops generously with cigarettes. Many must have contracted the habit during the war. Cigarette smoking has increased progressively since then. Few women smoked before the first war. Even in the 1920's it was considered rather fast to do so. The pandemic of influenza in 1919 often affected the lungs. If this was a predisposing cause, it should have produced a mortality that ceased and was not progressive. It may have been the factor in some cancers of the pulmonary parenchyma.

Chimney-sweep's cancer was attributed to its rightful cause long before we knew the nature of carcinogenetic agents. Cigarette smoking has increased in Great Britain, the United States and Australia. Can anyone suggest any other possible cause of the increase in cancer of the lung? It must be something common to these three countries that was not in operation before the first World War. I cannot think of any.

What is to be done? The tobacco companies can play an important role in encouraging people to smoke pipes and cigars instead of cigarettes. If they do not do so, legislation which is inevitable if the disease is not controlled, may cripple them. After all, their directors and staff, if cigarette smokers, must be suffering with the rest of the community unless, getting their smoking cheaply, they can throw away half perhaps of each cigarette.

Why do young people start smoking? It is merely a form of ostentation. There is no hardship in not learning to smoke, there is no necessity to do so. New undergraduates at the university should be strongly advised not to smoke cigarettes by the medical officer who interviews them.

From the trachea to the bronchioles, the normal epithelium is columnar and ciliated. Metaplasia to a squamous epithelium may be seen occasionally in bronchiectatic cavities. The increase in carcinoma of the lung is, I understand, chiefly in squamous epitheliomata. Two factors may therefore be concerned, one converting the columnar epithelium into squamous, the other initiating the malignancy in the latter. In inversion of the uterus, the columnar epithelium now perhaps exposed in the vagina may undergo metaplasia, but malignancy of squamous type does not, necessarily at least, follow. Columnar epithelium requires a loose stroma to support it, as in the alimentary canal and less so in the bronchi. If the stroma becomes dense, as in the skin, will the epithelium become squamous? We see, in the liver, such a change of type. When juicy hepatic cells become surrounded by secondary fibrous tissue, they become converted into smaller cells to form what are called new bile channels. Exposure to drying, as in the inverted and exposed uterus, may lead to metaplasia. Does the constant flow of mucus protect the nose and the trachea? Does hot air dry the bronchioles? It would be well worth while to see whether, in habitual cigarette smokers who inhale, there are areas of metaplasia in the bronchial epithelium which are not malignant, and whether such do not occur in control non-smokers.

Another point of unusual interest is how the carcinogenetic factor in this and other cancers is able to effect changes in the exposed cells which are "remembered" and are accumulative so that, after many generations, perhaps thousands in the case of the skin of the lips, the descendants of the sensitized cells may become malignant, even though the carcinogenic agent has long ceased to operate. Is it, as I have suggested elsewhere, that these deleterious factors cause premature aging of the cells to such an extent that hitherto dormant and recessive gametogenic factors in the cells concerned assert themselves, the previously dominant somatic factors being no longer able to control them? Is such, indeed, the nature of cancer?

Yours, etc.,

Adelaide. J. B. CLELAND.
September 27, 1959.

MEDICINE AND ATOMIC ENERGY.

SIR: The letters of Dr. D. Everingham and Dr. S. J. Cantor on the problems of war and peace prompt the following remarks.

The Australian and New Zealand Congress for International Cooperation and Disarmament and Festival of the Arts is to take place in Melbourne, from November 7 to 14, 1959.

I have not read any official statement in the Journal about this congress. Those members of the medical profession who are concerned to help improve international relations may feel inclined to support and attend this congress, whose lofty aims must have a strong appeal to all mankind irrespective of the individual political and religious beliefs. I would like to see the question of official representation of the British Medical Association taken up by the Federal Council, if it has not already done so. A delegation comprising a member of each State Branch, together with official representation in the Federal Council, would, I am sure, create goodwill and help to promote the cause of peace.

Doctors who wish to obtain further information on the various activities associated with the congress should write to either of the following:

The Secretary, N.S.W. Preparatory Committee, Congress for International Cooperation and Disarmament, Room 18, 421 Sussex Street, Sydney, N.S.W.

The Organizing Secretary, Australian and New Zealand Congress for International Cooperation and Disarmament, 259 Collins Street, Melbourne, Victoria.

Yours, etc.,

190 Macquarie Street, Hobart, Tasmania.
September 25, 1959. D. M. L. FINLAY.

HARE LIP AND CLEFT PALATE.

SIR: In "Current Comment" for June 13, 1959, on the subject of "Hare Lip and Cleft Palate" it is stated than many plastic surgeons violently disagree with my operation for double hare lip, since it produces an unpleasant tall lip tight from side to side. The first statement is correct; as I recently pointed out in your paper, many plastic surgeons violently object to my operation for hypospadias, and many orthopædic surgeons to my active treatment of talipes and congenital dislocation of the hips. Violent objection from those who use established methods is the accolade given to any new idea, and it is quite right that this should be so. But the second statement is nonsense, as anyone who looks up the pictures of results in *Annals of the Royal College of Surgeons of England*, September, 1949, at page 169, will see. My formula, if exactly used, gives a shorter, thicker and more mobile lip than any other, since by it alone are the actual ends of the cleft orbicularis oris muscle joined. I suggest it is possible that Mr. Oldfield recommends it because he understands it and has seen the results.

As a point of editorial policy, I would suggest that anonymous criticism should be left to the universal oracles of the popular Press, and to literary gents who have scores to settle; it should have no place in medical writings. The value of a criticism depends on what the maker of it has done, seen and read; and to the latter point a list of references gives some clue.

Yours, etc.,

46 Harley Street, London, W.1, England.
September 30, 1959. DENIS BROWNE.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR NOVEMBER, 1959.

THE Melbourne Medical Post-Graduate Committee announces the following programme for November, 1959.

Symposium on Carcinoma of the Cervix Uteri.

On November 7, the Melbourne Medical Post-Graduate Committee will conduct a symposium on carcinoma of the cervix uteri from 11 a.m. till 2.30 p.m. at the Royal Melbourne Hospital, which all medical practitioners are invited to attend. The programme has been arranged in consulta-

tion with the Anti-Cancer Council of Victoria, and will consist of nine quarter-hour lectures, as set out in a previous issue of this Journal. Discussion will follow the presentation of papers in the Main Lecture Theatre. Lunch will be served in the hospital's cafeteria. Attendance and lunch will be without fee, but the Committee requests that notification be given of intention to be present.

Country Courses.

The following country courses will complete the Committee's programmes for the year:

Traralgon.—On November 7, at the Base Hospital, Traralgon, the following course will be given: 2.30 p.m., "Hypertension", Professor J. Hayden; 4 p.m., "Diabetes", Dr. J. R. Stawell; 8 p.m., "Recent Advances in Pædiatrics", Dr. H. Williams; 9 p.m., quiz session. The local secretary is Dr. J. E. Joseph, 237 Prince's Highway, Morwell.

Bendigo.—On November 14, at the Base Hospital, Bendigo, the following course will be given: 2 p.m., "Forceps Delivery", Dr. P. Jeffery; 3 p.m., "The Coughing Child", Dr. H. Williams; 4.15 p.m., "Anal Conditions", Mr. E. S. R. Hughes. The local secretary is Dr. M. Clark, 98 Mitchell Street, Bendigo.

Mooroopna.—On November 21, at the Base Hospital, Mooroopna, the following course will be given: 2.30 p.m., "Maternal Mortality", Professor L. Townsend; 4.30 p.m., "Cardiac Failure", Dr. J. Cahill. Dr. B. R. Schloeffel, Orr Street, Shepparton, is local secretary.

Portland.—On November 21, at Portland, at 3.45 p.m., a symposium on "Anæsthetic and Surgical Procedure in Obstetrics" will be given by Dr. R. M. Rome and Dr. G. Robinson. The local secretary is Dr. R. R. Sobey, 6 Spence Street, Warrnambool.

Ballarat.—On November 26, at Craig's Hotel, Ballarat, at 8 p.m., Mr. G. Newman-Morris will discuss "Bleeding from the Nipple and Other Breast Conditions". The local secretary is Dr. Ian Goy, Base Hospital, Ballarat.

Fees.—The fees for attendance at the above-mentioned courses are at the rate of 15s. per lecture, but those who have paid an annual subscription to the Post-Graduate Committee are invited without further charge.

Flinders Naval Depot.

On November 18, at 2.30 p.m., at Flinders Naval Depot, Mr. B. T. Keon-Cohen will discuss "Metatarsalgia". This lecture is being given by arrangement with the Royal Australian Navy.

Information.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne. Telephones: FB 2547, 2548.

The College of Radiologists of Australasia.

RESULTS OF EXAMINATION FOR MEMBERSHIP.

THE names of the successful candidates in Part II of the examinations for membership of the College of Radiologists of Australasia, held in August, 1959, are as follows:

In radiodiagnosis: Dr. C. J. Adair, Queensland; Dr. G. T. Benness, New South Wales.

In radiotherapy: Dr. R. G. Bourne, Queensland; Dr. J. M. Bradley, Victoria.

Notes and News.

The Halford Oration.

The Halford Oration will be delivered on Thursday, October 29, 1959, at 8 p.m., in the Anatomy School, University of Melbourne. The orator is Sir William Upjohn, who will take as his subject "Curiosity".

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 19, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2	1(1)	2(1)	..	1(1)	..	..	..	6
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	2	..	..	..	8	..	10
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	1	..	..	..	1	..	..	..	2
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	3	9(9)	5(4)	..	1(1)	2	1	2	23
Diphtheria	..	..	..	..	1	..	..	..	1
Dysentery (Bacillary)	..	..	..	3(3)	2(2)	..	2	..	7
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	72(26)	15(10)	21(3)	9(7)	2	..	2	..	121
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	2	..	2
Leptospirosis	..	..	10	..	..	..	..	..	10
Malaria	..	..	1	..	..	..	..	..	1
Meningococcal Infection	3(1)	..	1(1)	..	..	2(1)	..	..	6
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1(1)	..	..	..	..	..	..	..	1
Puerperal Fever	4(1)	..	..	..	..	..	..	..	4
Rubella	..	27(15)	..	..	6(5)	..	..	..	33
Salmonella Infection	4(3)	7(3)	6(5)	11(6)	..	3	..	..	31
Scarlet Fever	..	..	1	..	..	..	..	..	1
Smallpox	..	1	..	..	..	..	19	..	20
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	32(27)	24(17)	10(4)	3(3)	9(4)	6(3)	1	..	85
Typhoid Fever	..	..	1(1)	1(1)	..	..	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The Royal Australasian College of Physicians.

MEETING OF THE VICTORIAN FELLOWS AND MEMBERS.

THE Victorian Fellows and Members of The Royal Australasian College of Physicians, in association with the Victorian Branch of the Australasian Association of Psychiatrists, will hold a Scientific Meeting at the Repatriation General Hospital, Heidelberg, on Saturday, November 14, 1959. The programme is as follows: 11.30 a.m., "Compensation Neurosis", Dr. Guy Springthorpe; 12 noon, "Some Aspects of Intracranial Hæmorrhage", Dr. A. C. Schwieger; 1.45 p.m., "Chemopallidectomy in Parkinsonism", Mr. R. S. Hooper; 2.15 p.m., "Experiences with 'Marsilid'", Dr. John F. Williams; 2.45 p.m., "The Myopathies", Dr. John Billings; 3.45 p.m., "Delirium", Dr. John Cade; 4.15 p.m., "Pain Syndromes in the Hand", Dr. Peter Ebeling.

Notice.

THE CHILDREN'S MEDICAL RESEARCH FOUNDATION OF N.S.W.

THE following is a list of donations to the Children's Medical Research Foundation of N.S.W. received from members of the medical profession in the period September 16 to October 13, 1959.

Dr. Shirley Brown (further): £200.

Professor and Mrs. Lorimer Dods (further): £150.

Dr. Donald Vickery (further): £100.

Dr. Peter Bishop (further): £50.

Dr. A. Thornton Taylor (further): £26 5s.

Dr. M. L. Edwards (further), Dr. D. G. Hamilton (further), Dr. M. Sofer Schreiber (further), Dr. and Mrs. J. A. L. Allen, Dr. J. C. Fulton (further), Dr. F. M. Hooper (further): £25.

Dr. P. A. Tomlinson (further): £21.

Dr. and Mrs. Douglas Cohen (further), Dr. R. J. G. Erby (further): £20.

Dr. Irene Sebire: £12.

Dr. A. K. Barrett (further), Dr. Bryan Dowd (further), Dr. and Mrs. Gordon Cousins, Dr. Gordon Colvin (further), Dr. John Beveridge (further): £10 10s.

Dr. A. Chancellor (further), Dr. R. H. Vines (further), Dr. F. W. Traill (further): £10.

Dr. Philip Oystragh, Dr. I. E. Leighton and Dr. D. W. Bruce (further), Dr. E. C. Blomfield (further), Dr. Lorna Ford (further), Dr. L. Cohn (further), Dr. Keith Barry (further), Dr. F. C. McCredie (further), Dr. George Selby, Dr. and Mrs. Bruce Symonds (further), Dr. and Mrs. D. A. Ferguson (further), Dr. S. Kotowicz: £5 5s.

Dr. H. W. Austin (further), Dr. D. R. Reid (further): £5 0s. 6d.

Dr. and Mrs. Alan Owen (further), Dr. Gregory McL. Blaxland (further), Dr. V. J. McGovern (further): £5.

Dr. John Church (further): £3 3s.

Dr. R. G. B. Cameron (further): £2 2s. 6d.

Dr. David Magill, Dr. T. S. Douglas (further), Dr. P. E. I. Lewis: £2 2s.

Dr. and Mrs. J. A. Carnahan (further): £1 0s. 6d.

Previously acknowledged: £8491 5s. 4d. Total received to date: £9418 8s. 4d.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Cooke, Ian Douglas, M.B., B.S., 1958 (Univ. Sydney), King George V Hospital, Camperdown.

Bradhurst, Peter Graham, M.B., B.S., 1959 (Univ. Sydney), Prince Henry Hospital, Little Bay.

Deaths.

THE following deaths have been announced:

MANNING.—Ian Garnet Manning, on October 10, 1959, at Sydney.

PATTERSON.—George William Patterson, on October 7, 1959, at Beaumaris, Victoria.

Diary for the Month.

OCTOBER 27.—New South Wales Branch, B.M.A.: Hospitals Committee.

OCTOBER 28.—Victorian Branch, B.M.A.: Branch Council.

OCTOBER 29.—South Australian Branch, B.M.A.: Scientific Meeting.

OCTOBER 31.—New South Wales Branch, B.M.A.: Branch Meeting.

NOVEMBER 3.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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